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A NEW FORM OF CONGENITAL HEMATOPORPHYRIA: OLIGOCHROMEMIA PORPHYRINURIA (MEGALOSPLENICA CONGENITA) *

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In this paper, we report a peculiar form of congenital hematoporphyria which hitherto has been undescribed. The name "oligochromemia porphyrinuria (megalosplenica congenita)" is suggested. The characteristic features of the conditions are:

1. Congenital hematoporphyria, that is, congenital porphyrinuria [1] with cutaneous sensitivity to light as its sequelum; (2) onset at birth; (3) enlarged spleen at birth with subsequent splenomegaly; (4) chlorotic type of anemia; (5) fatal termination; (6) familial factor (presence of entire syndrome in each of the affected members).

The cases described here represent the earliest form of congenital porphyria on record. The onset at birth would tend to support the theory of an endogenous disorder of metabolism. The excretion of an intensely red urine, rich in porphyrins and the sensitivity to light manifested by the typical hydroa lesions, appear shortly after birth. The complete symptom triad of congenital porphyria includes the purplish pigmentation of the milk teeth, although this sign is less constant. The next earliest case on record has been described by Ashby,[2] and was first

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* From the Department of Pediatrics, the Medical College, Tohoku Imperial University. Preliminary paper: A Form of Porphyria Congenita Not Yet Described in the Literature, read at the Twenty-Fifth General Meeting of the Japanese Pediatric Society, Tokyo, April, 1920. The dermatological report of our case will be made by Professor Toyama, of the dermatological department, in another journal.

1. In this paper, the term "congenital porphyrinuria" is used in a meaning different from "congenital hematoporphyria." The former means more excretion of porphyrin in the urine as a congenital abnormality without reference to other symptoms, while the latter denotes congenital porphyrinuria with sensitivity to light. Congenital porphyrinuria may be a disease itself without sensitivity to light, just as hydroa aestivale occurs without any accompaniment of porphyrin excretion. In this paper the shorter word "porphyria" will be used throughout instead of hematoporphyria, as that word has already been used by some authors. The term porphyria was likewise used in our preliminary report.

2. Ashby, H. T.: A Case of Hematoporphyria Congenita, Brit. M. J. 803, 1924.

observed at the age of 1 year. The infant reported by us (S. M.), when seen for the first time at the age of 3 months, was suffering with intense porphyrinuria and the peculiar skin affection.

The spleen, which is very large at birth, increases rapidly in size. Very few descriptions of congenital porphyria mention enlargement of the spleen.[3] This fact is commented on by Ward,[3] and it would seem that even the persistence of the disease over many years fails to produce any definite splenic enlargement. Günther [4] describes a patient with congenital porphyria with urinary symptoms and hydroa aestivale at the age of 20 months, but in whom there was no enlargement of the spleen until the age of 23.[5] Enlargement of the spleen is mentioned in a 5 year old boy reported by Konigstein and Hess.[6] The patient had syphilis, and the spleen was only slightly enlarged. The only case of congenital porphyria with splenomegaly is Shultz's [7] patient, who seems to have been suffering from attacks of blisters since he was 3 months of age. When this patient was 29, the cutaneous affection was very severe and accompanied with high fever, but the enlargement of the spleen was not noticed until two years later. During the next two years, a tremendous increase in size occurred, and at death the organ extended into the pelvis. Unfortunately, there is no account of the blood changes before and after enlargement. The second case of congenital porphyria described in Japan was that of a girl, aged 18 years, in whom no enlargement of the spleen was mentioned.[8]

The blood picture presents nothing abnormal except the great reduction in hemoglobin content. The number of red cells and the hemoglobin remained fairly constant throughout the course of the disease except that at the end the amount of hemoglobin progressively diminished. These findings are in striking contrast to the blood picture in most of the previously reported cases of porphyria congenita. The cases of Mackey and Garrod,[3] Ashby,[2] Kitagawa,[8] and many others, showed no abnormal condition of the blood. It is for this reason that Garrod [9] stated that "there is no necessary connection between excess of hematoporphyrin

3. Ward: Clinical Hematology, 1914, p. 266. Mackey, L., and Garrod, A. E.: On Congenital Porphyrinuria, Associated with Hydroa Aestivale and Pink Teeth, Quart. J. Med. **15**:325, 1921-1922.

4. Günther, H.: Die Hamatoporphyrie, Deutsche Arch. f. klin. Med. **105**:130, 1912.

5. Günther, H.: Die klinischen Symptome der Lichtuberempfindlichkeit, Dermat. Wchnschr. **68**:185, 1919.

6. Konigstein, H., and Hess, L.: Zur Klinik und Aetiologie einer bisher nicht beobachteten Form von Hautgangran, Dermat. Ztschr. **17**:913, 1910.

7. Schultz, quoted by Günther, H.: Footnote 4, p. 126.

8. Kitagawa, K.: Twenty-Fifth Congress of the Japanese Dermatological Association in Nagoya, March, 1925.

9. Garrod, A. E.: The Urinary Pigments in Their Pathological Aspects, Lancet **2**:1328, 1900.

in the urine and excessive hemolysis." In Günther's case,[10] the blood count was normal, and the anemia (reduced red cell count and reduced hemoglobin) did not appear until late in the disease. He writes that the normal number of red cells without evidences of regeneration speaks against the theory of the origin of porphyrin through destruction of hemoglobin. There is not, as far as we know, another reference in the literature to the chlorotic type of anemia or a blood picture in which oliogochromemia is the only observation.

The disease here described is fatal, without any apparent complication. Our patient (S. M.) lived for sixteen months and his brother is said to have died at the age of 1½ years. This seems especially interesting, as none of the other reported cases terminated early in life. In fact, Ward [8] and Günther [10] state that hematoporphyria congenita is rarely fatal. Ashby's patient remained in good health as long as precautions against exposure to excessive sunlight were taken. Mackey and Garrod's patient, who was one of the youngest described, was quite bright and well formed at the age of 6. The earliest deaths reported of patients who had suffered from porphyria since early childhood were at the ages of 15, 31, and 34 years respectively.[11] It is in this respect that our form of the disease differs so strikingly from the other cases of porphyria congenita.

The disease is congenital (not hereditary), and is definitely familial. We wish to emphasize especially the occurrence of all the before-mentioned symptoms in each child affected with the disease. Thus the symptoms are not separable, but form one clinical entity.

CASE REPORT

S. M., a boy, aged 3½ months, came to our dispensary, Nov. 4, 1919, with the complaints of red urine, abdominal tumor and peculiar scar-like eruptions on the face.

History.—It was noted early that the child was very pale, and about fifty days after birth the mother observed the reddish brown color of the urine. The abdominal tumor was likewise apparent shortly after birth. During the last twenty days the child had suffered from a peculiar eruption, which appeared at first as small vesicles. The urine had continued to be red, although the color, which was subject to slight changes of intensity, recently seemed darker.

Physical Examination.—The child weighed 6,000 Gm.,[12] which was quite normal for a Japanese child of that age. The skin and mucous membranes were pale with a slightly brownish tinge. The swollen abdomen was due to the greatly enlarged spleen (5 cm. from the costal border to the tip), which was hard and relatively freely movable. The liver was palpable, 3 cm. below the costal

10. Günther, H.: Die Bedeutung der Hamatoporphyrine, Physiol. u. Pathol. Lubarsch-Ostertag **20**:757, 1922.

11. Anderson, cited by Mackey and Garrod: Footnote 3, p. 319.

12. Weight of a normal male Japanese infant, aged 3 and 4 months, is 5,470 and 6,050 Gm. respectively. Mishama, M.: Das Wachstum des Kindes in Japan, 1902.

border in the mammillary line and of normal consistency. The eruption on the face consisted of numerous lesions occurring chiefly on the cheeks, leaving the chin and forehead entirely free. They resembled scratched spots deeply excoriated, and here and there were covered with small crusts. No blisters were seen. The urine was reddish, but neither the guaiac nor the benzidine test was positive, in spite of repeated examinations.

Fig. 1.—Photograph taken shortly after S. M.'s second admission. The outline of the spleen is shown in black.

The lymph nodes were not enlarged. No hemorrhagic spots were seen on the skin or mucous membranes. According to the mother, the family physician had treated the child with antisyphilitic medication for some time previous to his visit to our dispensary. His Wassermann, tuberculin and syphilitic tests were negative.

Family History.—There was nothing to report of particular interest concerning the parents. There was no consanguinity. The grandparents on both sides were

still healthy, and there was no history of tuberculosis or of syphilis. The Wassermann tests of the parents were negative. There had been no miscarriages. The first child, a normal boy, died of acute meningitis in the ninth month. The second child was a girl, who had spina befida and died forty days after birth. The third child was a boy, 11 years of age, who was living and quite healthy. The fourth child was a girl, who died at the age of 6 months of some cutaneous disease (eruptions mainly on the face). According to the mother, the child had red urine, a large tumor in the left side of the abdomen, and large lymph nodes. The fifth child, a normal boy, died of pneumonia one year after birth. The sixth child, a boy, died of the same cutaneous disease as the fourth child. He was pale, had red urine and large lymph nodes in both armpits. The mother noticed a large tumor below the left costal border. He lived for one and one-half years, and received antisyphilitic medication for some time previous to his death. The seventh child was the infant in question.

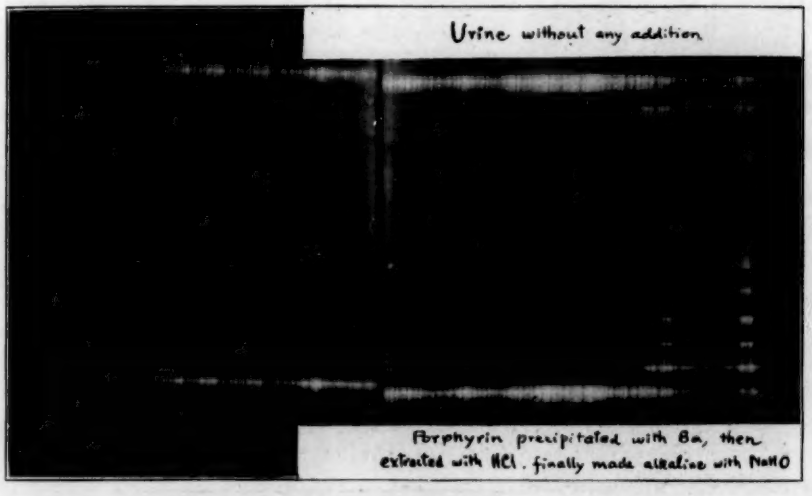

Fig. 2.—Spectra of patient's urine showing absorption bands of porphyrin.

Course in the Hospital.—The patient's first stay in our department was of about three months' duration. He gained in weight satisfactorily. His temperature was irregular with slight elevations.

The urine was clear, slightly acid, always dark red, although the color fluctuated in intensity. Hemoglobin, albumin, sugar, acetone, diacetic acid, bilirubin, urobilin and diazo reactions were negative; indican reaction was one plus. There were no casts, red cells or leukocytes. The urine was repeatedly examined and these tests were always the same.

The stools contained no ova of parasites. Tests for blood were negative. Porphyrin was demonstrated in large amounts by the method of H. Fischer.[13] As controls, the stools of fifteen patients were examined by the same method but no porphyrin was found.

On admission the spleen was smooth, hard and measured 5 cm. from the costal border to the tip. Twenty days later this had increased to 7 cm.; ten days later to 9 cm., and later to 9.5 cm. It was from 6 to 6.5 cm. in width.

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13. Fischer, H.: Uber das Kotporphyrin, Ztschr. f. phys. Chem. **96**:161, 1915-1916.

While the size of the spleen progressively increased, that of the liver gradually diminished. It was 3 cm. below the costal margin on admission, but one month later it could not be palpated.

There were no new eruptions until two months and twenty days after admission, when new blisters began to appear on the face. Only one small purpuric spot was noted by Dr. Toyama, professor of dermatology. This was situated in the left infraorbital region beside the radix of the nose. It was very small, about the size of a pinhead, and consisted of a great number of minute hemorrhagic points.

Except for a diminished hemoglobin content, the blood was not abnormal. There were no nucleated cells, no poikilocytosis, no pathologic anisocytosis and no polychromatophylia. The platelets were normal. The color index was 0.6.

When the patient was brought back to the hospital in 1920 at the age of 15 months, his pallor was very striking. The spleen was larger, and the urine still dark red in color. His mother said that he had excreted this type of urine since

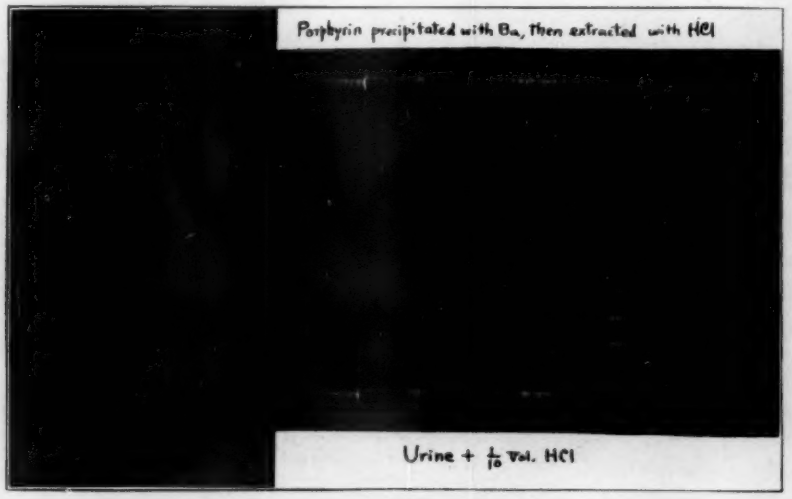

Fig. 3.—Spectra of patient's urine showing absorption bands of porphyrin.

discharge. He remained with us for twenty-six days and during this time we observed the following changes:

He had now milk teeth, eight incisors and four premolars in all; they were normal in shape. What appeared most extraordinary to us was the purplish discoloration of these teeth. From what we could learn from his mother, the purple color was present from the time of eruption.

The skin eruptions were very striking on all the exposed parts, namely, on the head, face, hands and feet. Four large ulcers and many smaller ones were present on the face. Some were very deep (1.5 cm.) and were covered with a seropurulent fluid. One or two fresh vesicles were also seen. On the back of each hand, especially near the metacarpalphalangeal joints, were several large ulcers. They occurred also on the fingers and toes and below both the internal malleoli. There was some destruction of the nails. No eruption was present elsewhere on the body. These ulcers on the face and on the head later became quite extensive. It seemed to be definitely established that these lesions were the result of sensitivity of the skin to sunlight.

Professor Koyanagi, of the ophthalmology department, found nothing abnormal about the patient's eyes except anemia of the disks.

It was only in the latter part of the child's second stay that any unusual elevations of temperature occurred, when it varied between 37 and 39 C. occasionally reaching 40 C. (104 F.). There was occasional vomiting, but the patient's appetite remained good and he gained in weight slightly. It was not until one week previous to discharge that his general condition began to suffer for the first time. At this time the hemoglobin fell to 27 per cent (Sahli). The red cell count remained about the same, 4,640,000, and the leukocytes numbered 11,000. As his general condition became progressively worse, his mother insisted on taking him home. He died ten days later, and permission for necropsy could not be obtained.

PATHOGENESIS OF THE NEW FORM

The features of other cases reported of congenital porphyria and those of our cases are illustrated in the table.

Two theories of pathogenesis of this new form of congenital porphyria are suggested. Although enlargement of the spleen is rarely

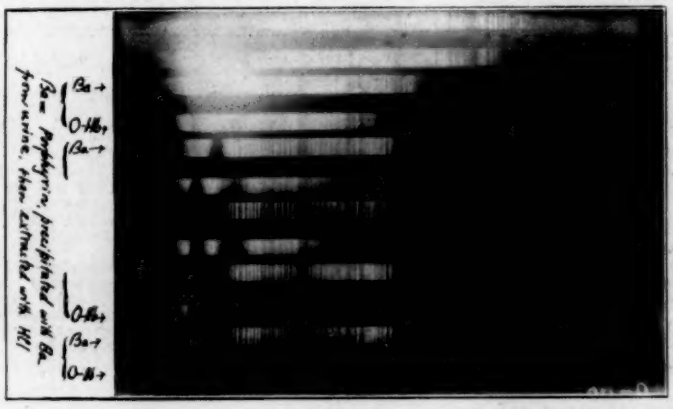

Fig. 4.—Spectra of patient's urine showing absorption bands of porphyrin.

mentioned, it is possible that this occurs late in the disease, as in Günther's case. If this is true, then our new form may simply represent an extraordinary fatal form of the ordinary type of congenital porphyria. Against this explanation is the marked difference in blood findings. The production of excessive amounts of porphyria is usually ascribed to hepatic insufficiency and not to any disorder of hematopoiesis. This supposition is corroborated by the presence of a normal blood picture in patients suffering from this disease. The marked anemia of our patients might well be explained as resulting from excessive "hemoglobinolytic" activity of the spleen. The hemoglobin is thus reduced to form large amounts of porphyrins. The fatal outcome is not a result of the presence of porphyrins, but of the severe anemia. This was true clinically, as the child made satisfactory progress until the amount of the hemoglobin was reduced to 27 per cent. The persistence of a normal red

cell count supports the view that only the pigment is affected. The enlargement of the lymph nodes might possibly have been due to the formation of hemolymph glands which partially assumed the function of the spleen. However, the rarity of these structures in the human body is well recognized.

Despite the excellent investigations on the biologic and chemical properties of porphyrins,[14] it seems unnecessary to change the beforementioned explanations. It is only important to add that the "hemoglobinolytic" activity of the spleen may mean, rather, a primary failure of synthesis of hemoglobin resulting from a congenital defect of the organ. Günther has lately made the interesting supposition that porphyrins are the material from which hemoglobin is built. The administration of iron and the application of ointments to the skin

Cases of Congenital Porphyria

Type	Porphyrin in Urine	Porphyrin in Stool	Sensitivity to Light	Deposition of Porphyria		Spleen	Blood	Outcome
				Permanent Teeth	Milk Teeth			
Porphyria congenita	+	+?	+	—	— or +	Normal	Normal (Red cell count normal; hemoglobin normal)	Rarely fatal
Oligochromemia porphyrinuria (megalosplenica) congenita	+	+	+	Patients died before eruption of permanent teeth	— or +	Enlarged	Oligochromemia (red cell count normal; hemoglobin markedly reduced)	Death in the first two years of life

was the only therapy used. None of the treatments reported[15] have any curative value. Applications of alcoholic solutions of tannic or salicylic acids appear beneficial.[16] It would seem now that total extirpation of the spleen might be an effective method of combating the disease. In our laboratory, Nitsu and Tokuye kept young rabbits in boxes with ultrazin glass[17] for some time, and came to the preliminary conclusion that such animals showed no essential difference from control animals in respect to growth and blood count. Such treatment in a large chamber may be practical for the prevention of cutaneous lesions in infant suffering from hematoporphyria.

14. Compare the papers of H. Fischer, O. Schumm, I. Snapper, and their co-workers.

15. Günther (footnote 10, pp. 762-763).

16. Meyer and Amster: Ueber Lichtschutz, Deutsche med. Wchnschr., 1925.

17. Ultrazin, a substance prepared by S. Sakurayi of the Institute for Physical and Chemical Research, Tokyo. The ultrazin glass prevents the transmission of the ultraviolet rays from 4,300 A° on.

CONCLUSION

In common with other cases of congenita porphyria, our case has only two important symptoms, namely, sensitivity to light and the excretion of porphyrins in the urine. In addition, there are congenital splenomegaly and a chlorotic type of anemia. The course is fatal in contrast to the hitherto reported form of porphyria congenita. Thus, it is practically a disease of infants. These symptoms form one clinical entity, and the disease might well be called "oligochromemia porphyrinuria (megalosplenica congenita)."

THE SICKLE CELL PHENOMENON *

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AND
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DETROIT

These observations were undertaken as a part of a study of some forms of hemolytic anemia, and were prompted especially by the receipt from Dr. Grulee of a film showing, in a case diagnosed as sickle cell anemia, skull changes similar to those described by us [1] last year.

Our hospital clientele includes many negroes, and for some ten months past the blood of all colored children admitted has been examined for sickle cells, and for evidence of any characteristic anemia in patients whose blood shows these forms. So far as possible, the blood of the parents and other relatives has been examined also, and inquiries have been made as to a history of any peculiar symptoms suggestive of anemia, and of leg ulcers.

In all, the blood of 400 colored hospital patients has been examined, and sickle cells have been found in 30, or 7.5 per cent. This is a much higher proportion than has been reported in the studies from the South.

In twenty-seven of these thirty patients, the hemoglobin (Dare) averaged 73.6 per cent, and the red cells 4,303,000. The highest figures were 90 per cent and 4,000,000 in a case of miliary tuberculosis, and 95 per cent and 5,300,000 in chorea; while the lowest were 45 per cent and 2,600,000 in advanced pulmonary tuberculosis.

In thirty-three patients without sickle cells, taken at random, the hemoglobin average was 69.7 per cent, and the red cell count 4,131,000; the highest figures being 100 per cent and 5,600,000 in chronic tonsillitis; the lowest hemoglobin 50 per cent in a patient with diarrhea, and the lowest red count 3,000,000 in one with pneumonia.

In other words, while moderate anemia seems to be the rule among our colored children, there is practically no difference in this regard between those with and those without sickle cells.

Fragility to salt solutions was determined in a number of cases. In twenty-one with sickle cells the average was: Beginning hemolysis at 0.39 per cent, complete at 0.25 per cent. Highest 0.45 to 0.35 per cent, in advanced tuberculosis, and lowest 0.35 to 0.2 per cent, in one of the

* Received for publication, June 24, 1926.
* From the Children's Hospital of Michigan.
* Read before the American Pediatric Society, Niagara Falls, Canada, May-June, 1926.

1. Cooley, T. B., and Lee, Pearl: A Series of Cases of Splenomegaly in Children, with Anemia and Peculiar Bone Changes, Tr. Am. J. Pediat. **37**:29, 1925.

cases of hemolytic anemia to be considered later. In twelve subjects without sickle cells the average was 0.4 to 0.22 per cent; highest 0.42 to 0.3 per cent, and lowest 0.35 to 0.2 per cent. Here again there is no difference between the two classes of patients. Reports of other observers have differed on this point.

FAMILY HISTORIES AND FAMILIAL SICKLING

We have not been able to make as complete a study of the families of the children with sickle cells as we should have liked, especially of the fathers, who are working men and hard to reach.

So far as family histories are concerned, we have as yet been wholly unable to obtain any history of symptoms of anemia or jaundice in any of these families. The question of the leg ulcers has particularly interested us. Not only do we get no history of anything of this character, but questioning physicians who have large practices among our colored people does not disclose that they are called on to treat any such conditions. With the high percentage of persons with sickle cells among our negroes, this is a surprising difference from the findings reported from the South.

Our findings regarding sickle cells in the parents also differ from those of Sydenstricker [2] and of Huck,[3] both of whom found evidence that the condition was transmitted equally by father and mother.

We have been able to examine fifteen mothers and six fathers. Of the mothers, eleven showed sickle cells, while of the fathers, sickle cells were found in only one. In two cases the blood of both parents was negative, and in the other two when the mother's blood was negative the father's was not obtained. In no case was the father's blood positive and the mother's negative.

Our observations on other members of the families are not extensive enough to be important.

OBSERVATIONS ON THE PATIENTS WITH SICKLE CELLS

These patients came to the hospital for a variety of conditions. None of them gave histories suggestive of chronic or recurrent anemia.

Two cases, to be described later, are excepted here. Aside from these, none of the children showed, on physical examination, any peculiar differences from other colored patients. Careful observation of their eyes failed to show the greenish yellow discoloration characteristic of hemolytic jaundice, which both Sydenstricker and Huck report as con-

2. Sydenstricker, V. P.; Mulherin, W. A., and Houseal, R. W.: Sickle Cell Anemia, Am. J. Dis. Child. **26**:132 (Aug.) 1923; Further Observations in Sickle Cell Anemia, J. A. M. A. **83**:12-17 (July 5) 1924.

3. Huck, John G.: Bull. Johns Hopkins Hosp. **34**:335 (Oct.) 1923.

stant in persons with sickle cells. There were no scars of leg ulcers in any. None had palpable spleens, nor was any special gland enlargement noted. None showed the peculiar skull conformation which we described last year. Roentgen-ray studies of skulls and long bones were negative. Urine and blood serum showed no evidence of hemolysis. The van den Bergh tests were negative. Blood pictures showed none of the characteristics of chronic anemia.

Four of the patients died: Two of miliary tuberculosis, one of peritonitis and septicemia, and one of pneumonia. The first three came to necropsy. No special findings were noted in any beyond those of the disease causing death—either in spleen, liver or bone marrow.

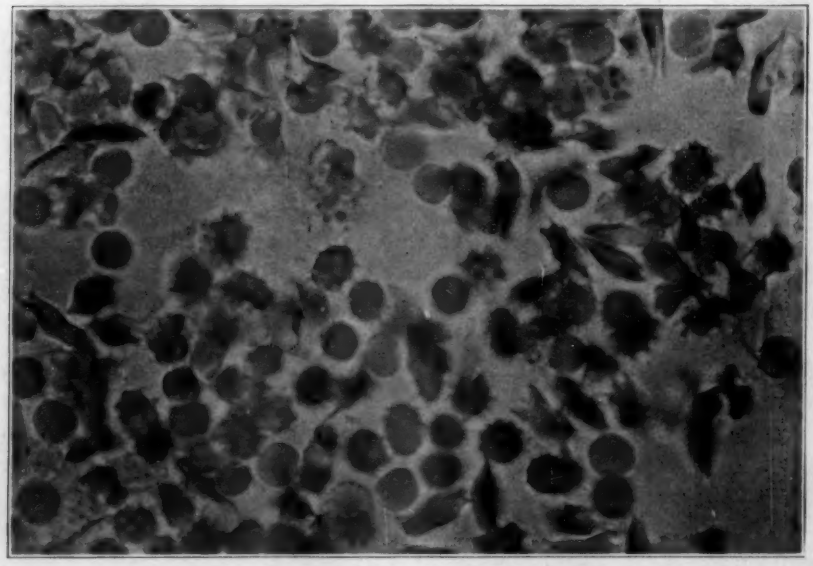

Fig. 1.—Moist preparation before and after placing in the incubator over night. From a tuberculous patient without clinical symptoms of anemia.

In general, there was nothing in the illnesses, symptomatology, physical findings, or clinical course, to distinguish any of these twenty-eight children from the ordinary negro patient, except the presence of sickle cells.

The two children, both girls, excepted above—H. R., aged 3 years, admitted for tonsillitis, and A. B., aged 5 years, admitted for tonsillitis and endocarditis—gave evidence of a mild grade of hemolytic jaundice, which was very slight in H. R., and more marked in A. B. (A. B. is the only child in both of whose parents we have found sickle cells.) Both showed the greenish yellow scleral pigmentation, pigmented serum with positive indirect van den Bergh (A. B.'s icteric index was 8 to 10) and

increased urobilin. They did not show the second pigment in blood and urine, which we have found in other forms of hemolytic jaundice. H. R.'s gastric acidity was diminished. A. B. had no free hydrochloric acid. Both had moderate leukocytosis. Fragility was slightly diminished, hemolysis being complete in each at 0.2 per cent. The red cells showed marked evidence of regeneration—polychromatophilia, reticulation, and varying numbers of normoblasts: all of these were more marked in A. B.'s blood. The leukocytes were not remarkable. Each showed 55 per cent hemoglobin, with 2,500,000 to 3,000,000 red cells. Neither has had crises of deglobulization, nor showers of normoblasts. Neither had subjective symptoms of anemia; the spleens were not palpable and

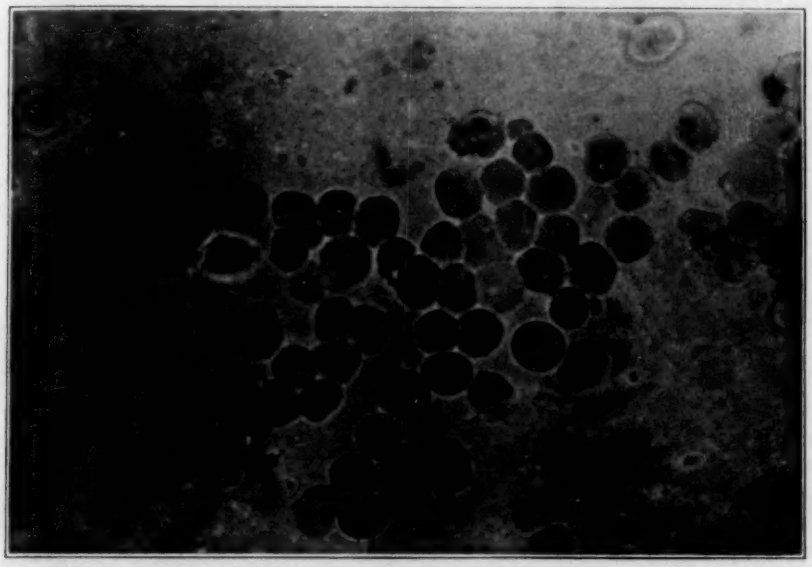

Fig. 2.—Disappearance of sickle cells in the same patient.

there were no gland swellings. No ulcers nor scars were found. Roentgenograms of A. B.'s skull and long bones show slight, rather doubtful signs of the thickening and porosity of the medullary portion which we have described before.

Clinically, we should consider these two as cases of very mild, atypical hemolytic jaundice, with no remarkable features.

OBSERVATIONS ON THE PHENOMENA OF SICKLING

In general, we can confirm the findings of Sydenstricker and others regarding the development of the sickle forms and their characteristics. We do not, however, find that they appear more rapidly, nor in greater proportion in A. B.'s blood than in that of some children without symp-

toms. Some bloods from symptomless children show sickle forms almost immediately, and 90 to 100 per cent in a few hours. We have observed great differences in the same blood at different examinations and, some times, of two preparations made at the same time and in the same way from the same patient, one will show many sickle forms and the others none. We have not ourselves been able to observe phagocytosis, though we do not doubt its occurrence.

We have made two observations, not elsewhere reported, which may be significant:

1. As is generally stated, the sickle cells remain for a considerable period unchanged in moist preparations kept at room temperature.

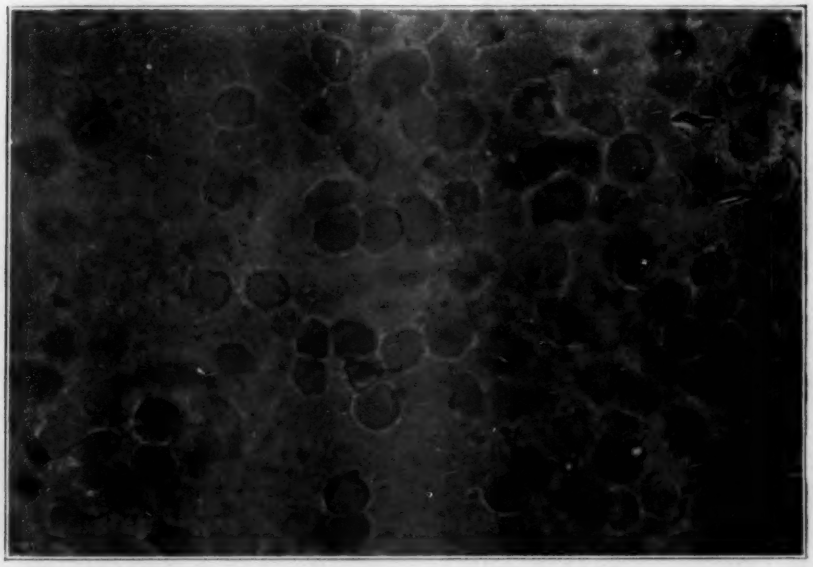

Fig. 3.—A. B.'s blood after two weeks of room temperature, showing disintegration of some cells, and return to the round form of others. This blood, when fresh, showed over 90 per cent of sickle forms.

though we have found that after two weeks most of them have returned to the round form. In the incubator, however, the sickle cells disappear over night, while the round cells are left. This is not a return to the round form. The cells are gone.

2. In A. B.'s blood, if it is placed in a test tube for twenty-four hours in the incubator, hemolysis occurs to a much greater degree than in normal blood. The same thing happens, in the same degree, if A. B.'s washed cells are mixed with normal serum, or with serum from a patient with acquired hemolytic jaundice. If washed cells from these other bloods are mixed with A. B.'s serum, hemolysis does not occur. This

observation is recent, and the experiment has been made with only one symptomless patient, in whom the results were negative.

A point has been made by some of the appearance of nucleated sickle cells. This, in our observations, is simply proportionate to the number of normoblasts in the blood, these forms taking the sickle shape just as the others do.

SUMMARY

Of 400 colored patients in the Children's Hospital, 30, or 7.5 per cent, were found to have sickle cells. Of the parents of the thirty children, fifteen mothers and six fathers were examined; eleven mothers and one father showed sickle cells, and in this one case the mother also showed them. With two exceptions, none of the children showed an anemia differing in any way from the average of a corresponding number of children without sickle cells. There was no history of anemic symptoms, nor of jaundice, in the children or their families, and no signs or history of leg ulcers; nor can we find that leg ulcers of the type described occur in the colored population at large. Yellow sclerae are not observed. Roentgenograms show nothing characteristic in the skull and long bones. Necropsies on three out of four children who died gave no significant findings. Two children have shown a mild grade of hemolytic jaundice. They had greenish-yellow sclerae, pigmented blood serum, positive indirect van den Bergh reaction, and increased urobilin. Gastric hydrochloric acid was diminished in one, and absent in the other. There were leukocytosis and moderate anemia with normoblasts, polychromatophilia and reticulation. The spleens were not enlarged, and no gland swellings were noted. There were no ulcers nor scars. Roentgenograms of the skull and long bones in one gave slight indication of changes like those we have noted in another form of chronic hemolytic anemia. Clinically, these two cases have nothing to suggest a separate disease entity.

Our studies of the phenomena of sickling confirm, in general, those of other observers. We have two new facts to add: (1) In preparations kept at incubator temperature, the sickle cells disappear rapidly from the blood, leaving the round cells behind; (2) the cells of one of the patients with hemolytic anemia are rapidly hemolyzed at incubator temperature in their own serums and in serums from normal bloods, while the serum of this patient is not hemolytic for normal cells. This test has not yet been applied to any number of sickle cell bloods. These two observations seem to imply a special vulnerability of the sickle cell.

CONCLUSIONS

The sickle cell condition is evidently very common in our negro population—possibly even more so in Detroit than in other sections in which it has been studied.

It is congenital, familial and hereditary, and possibly transmitted chiefly through the mother.

The presence of sickle cells in the blood does not in itself imply any essential anemia, active or latent. Sickle cells are common. Most of the subjects having them are as normal in all other ways as the rest of the colored population. The hemolytic jaundice occurring in these people is rare, and the two conditions should be distinguished. The term, "sickle cell anemia," should be reserved for patients with definite hemolytic anemia, and another term used for the condition without symptoms. "Sicklemia" would be descriptive, but this is a hybrid word. "Sacklemia," using the Greek root, would be proper, but of less obvious meaning.

Although our observations do not definitely bear it out, we think that there is enough evidence in the literature to justify the opinion that sickle cell anemia is probably a real disease entity, to be considered as another form of familial hemolytic jaundice; and that here, as in some other forms of anemia dependent on chronic hemolysis, there may be said to exist a hemolytic diathesis, due probably in this case to a special vulnerability of the red cells to some hemolytic agent. From this point of view the condition is important, both because it strengthens current views regarding familial factors in hemolytic anemias, and because it offers a ready source of material for study of the nature of the hemolytic processes at present not at all understood.

The subject offers two interesting points for speculation: 1. If, as Huck believes, sicklemia is a dominant mendelian characteristic, and it is now as common as it seems to be in Detroit, shall we not in a few generations have a negro population, the majority of whom show this peculiarity, and will not "sickle cell anemia" then be a common condition?

2. Could one arrive at the source of this interesting familial peculiarity? Might not men working in Africa, where the negro strains are still well separated, perhaps find a tribe in which sicklemia is the rule, and from which the condition was imported to this country?

ACQUISITION AND LOSS OF HYPERSENSITIVENESS IN EARLY LIFE*

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There are many points in which the manifestations of hypersensitiveness differ in infancy and in childhood from those encountered in adult life. It is our purpose to consider only those points which pertain to the acquisition and the loss of individual sensitivities.

There are certain generally accepted impressions which bear on this subject, which should be mentioned before studying detailed evidence more closely. In the first place, it is recognized that states of hypersensitiveness are much more frequently encountered in late infancy and early childhood than in adult life. This difference is admittedly largely due to the frequency of food idiosyncrasies at this age, which more than compensates for the very infrequent finding of hay-fever and asthma caused by hair or feathers. Furthermore, it is evident that the medical profession recognizes the transient character of these food idiosyncrasies, for they treat the finding by elimination only and assure the parents that the state will be outgrown. Some well-known pediatricians go so far as to forbid the inclusion of egg-white in the infant's diet until the age of 18 months, and to omit fish, nuts and fresh fruits until a proportionately later date, knowing that by so doing symptoms of allergy will be less often encountered. These general impressions suggest a change in the individual sensitivities manifest from year to year in children inheriting an allergic tendency.

During the last five years, a large number of these children have been studied in a special clinic at the Children's Hospital, together with some in private practice; from these cases it is proposed to present some more definite evidence bearing on this phase of allergy.

FOOD PROTEINS

The impression that hypersensitiveness to food proteins is most commonly encountered in early life has been mentioned. Just how often it occurs in adults is not known, but one would suppose that it is rare. A history was recently obtained of a man who unwittingly ingested

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* From the Medical Division of the Children's Hospital and the Department of Pediatrics, Harvard Medical School.

* Read before the Society for the Study of Asthma and Allied Conditions, Albany, April 2, 1926.

some fish at a dinner party, and caused great confusion by the severity of the asthma and giant urticaria which immediately followed. His story was that, as a child, he had drunk a can of glue on a bet, and as a result, had been unable to touch any fish thereafter. We have figures relating to the frequency of food sensitizations in childhood which are presented in chart 1. The subjects found to react to food proteins have been divided according to the year of age when tested, and these have been charted as percentage of total positives. The subjects studied in each year group have been graphed on the same chart as percentage of total subjects, to show that the difference in number of food cases per year of age is real and not a difference in clinic attendance. Subjects under 1 year have been omitted because so inadequately tested (chart 1). This chart shows that by far the greatest percentage of food cases is encountered in the second year, and that this percentage falls rapidly until by the sixth year it is one quarter that of the second. After the sixth year the percentage is unimportant.

The curve shown on this chart suggests that there must be a natural loss of sensitivity to food proteins during childhood. If one takes careful histories, the story is frequently elicited of food idiosyncrasies in early years with no subsequent evidences of allergy. Even in the short span of years that come under the pediatrician's observation, this loss of a food sensitization without any treatment is not infrequently encountered.

In our series, the shortest period required for the natural loss of reactivity to egg protein was two years. This occurred in a private patient (R. G.), who developed acute symptoms during the early months of the second year when offered foods containing egg. After this had occurred several times, egg was strictly omitted. At the age of 3 years and 4 months, the boy was tested because of asthma which had developed during the preceding six months. He was found negative to egg proteins and was therefore offered egg, which he took without symptoms. A more frequent course in the untreated is shown by the following case: P. W., a boy, aged 11 years, was seen in consultation because of a skin eruption thought to be possibly dependent on a food idiosyncrasy. There was a history that he had developed several severe attacks of giant urticaria when offered egg in the second year of life. For more than nine years egg had been very strictly eliminated from the diet, and the parents could remember no attacks of urticaria for several years preceding this visit. Never having seen a boy of this age able to maintain a strictly egg-free diet year after year, we concluded that he was no longer sensitive, and this belief was confirmed by obtaining negative egg tests. He was then offered this food, and within a week was eating an egg daily without symptoms. He still disliked them, but this is usually true in treated patients, even after they have taken large doses over a

long period. Sometimes the loss of sensitivity is far more gradual. Another child, L. C., aged 11 years, and with an almost identical history, except for occasional asthmatic attacks during the preceding five years, was also found to show negative scratch tests to the egg proteins. The last known occurrence of urticaria following the ingestion of egg had been at the age of 5 years, but urticaria sometimes accompanied her asthmatic attacks. The first day after the test, one-half teaspoonful of soft cooked egg caused some general itching and irritability. On the second day, a whole teaspoonful produced swelling of the eyes and face and some wheezing. The same dose repeated once again produced

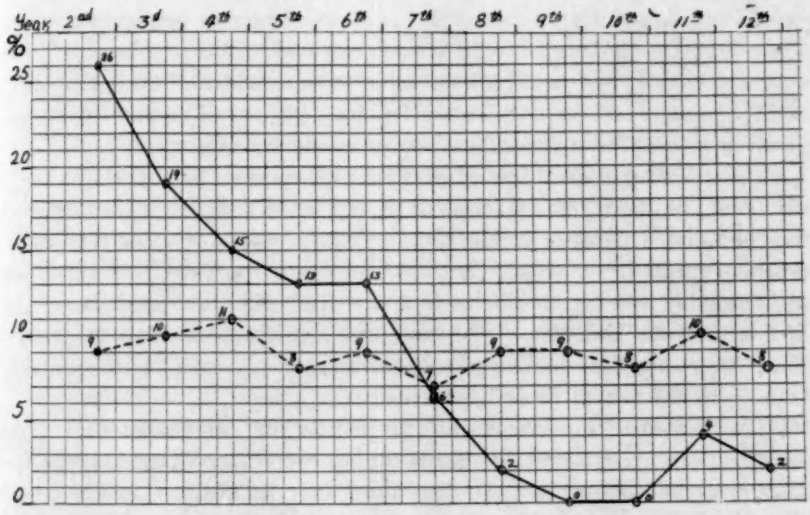

Chart 1.—Distribution of cases of hypersensitiveness to food proteins according to age. Based on fifty-seven positive cases. Food cases, straight line; total cases, broken line.

vomiting as well as the before-mentioned symptoms. A repetition of our scratch tests failed to produce any reaction, so intradermal tests were made with freshly prepared egg white dilutions, procured through Dr. Rackemann's office. Negative tests were obtained with these, even in a concentration of 1:10. The girl's serum also failed to transfer local egg white sensitivity, using the technic of Walzer and Kramer.[1]

It is not our purpose to discuss this discrepancy between protein tests and clinical symptoms, but the case is presented as one still maintaining a hypersensitiveness to egg-white of a known duration of ten years. Dr. Blackfan tells of the father of one of his patients who, in middle life, was still unable to touch any food containing egg.

1. Walzer, M., and Kramer, S. D.: J. Immunol. **10**:445 (Sept.) 1925.

These very different results bring us to the important conclusion that, although the tendency to outgrow food sensitizations does exist, it cannot be predicted when this result will take place in any given case. This point is considered of real importance, because it guides us in advising parents whose children are found hypersensitive to important food substances. Knowing that such sensitizations may persist throughout childhood, that strict elimination requires a very abnormal type of life, and that the child may be subject to repeated severe reactions if it is not carried out, we are led to advise treatment by the oral method at an early age. This advice can be given with enthusiasm in cases of milk or egg sensitization, because treatment with these substances is so simple and so regularly successful. It almost suggests negligence to see a boy of 8 years having suffered from occasional severe attacks of asthma over a period of six years, all traceable to the accidental taking of egg, and the parents still waiting for the fulfilment of the physician's promise, given in infancy, that the iodiosyncrasy would be outgrown.

The so-called natural loss of hypersensitiveness to food proteins may, of course, be the result of frequent though unrecognized small doses of the offending substance in the diet, and may, therefore, correspond to desensitization treatments. Egg and milk are the two food reactions most quickly lost in childhood and are the two eliminated from the diet with most difficulty. Fish and nut sensitizations tend to persist much later into life, and these substances are very easily and regularly kept from the diet of those hypersensitive.

The evidence thus far seems to justify the conclusion that food sensitizations are irregularly outgrown, but there may be more room for dispute as to whether such sensitizations may be acquired. The usual story is unquestionably that the reaction occurred on first contact, and milk idiosyncrasies are sometimes detected in the first weeks of life. Whether or not some of the subjects may have had a previous contact is hard to determine, but it is unwarranted to assume such a contact in all. Very occasionally, one does see a case which suggests the acquisition of a food idiosyncrasy, as, for example, the man referred to who drank the fish glue. In our whole series, not a single case was discovered in which an original food test was negative with a later one definitely positive, and with a confirming history of the first contact causing no symptoms, while later contacts did produce acute symptoms. We may, therefore, conclude that the acquisition of hypersensitivity to a food protein is an extremely unusual occurrence.

INHALANT PROTEINS

When the available information regarding hypersensitiveness to inhalent proteins is considered, a very different series of facts present themselves. Asthma is found to be infrequent in infancy, and hay-fever

rare before the sixth year. Furthermore, there is a strong tendency for a patient once hypersensitive to an inhalant to remain so over a long period of life. Physicians do not tell their adult asthma patients to avoid horse dander or pollen temporarily, and that the sensitivity will soon be outgrown. We cannot discuss the frequency with which such sensitizations are outgrown after the twelfth year, but it is observed infrequently before that age. One girl (R. C.) definitely lost a hypersensitivity to cat hair, both clinically and by test, some time between her sixth and eighth years. A boy (J. M.) reacted strongly to all the feather proteins at 9 years when having severe attacks of asthma. At 14 years he was found negative to all of these, and had had no asthma in two years.

Through the kindness of Dr. Blackfan and Dr. Koessler, the following case may be cited, showing clinically the loss of reactivity to horse dander between the ages of 10 and 17 years. A boy (C. K., Jr.) subject to eczema and egg idiosyncrasy in infancy, and successfully desensitized to egg-white by Dr. Blackfan, between his fifth and tenth years gradually developed both hay-fever and horse asthma. Contact with horses produced both urticaria and respiratory difficulty. By avoidance of contact with horses he kept free from symptoms, except in the pollen season, until the age of 17. At this time he visited Dr. Koessler, in Chicago, to determine whether it would be possible for him to train at West Point. Dr. Koessler, finding only a slight reaction to the strongest concentration of horse dander, advised him to visit a riding school and to experiment with close contact with horses. This was done, and no symptoms of either urticaria or asthma developed.

Chart 2 shows the distribution of inhalant protein cases between the first and twelfth years, on the same percentage basis as the food cases were represented in chart 1. This shows a striking absence of inhalant positives in infancy, with a rapid rise until the eighth year. This portion of the chart suggests a strong tendency toward the acquisition of inhalant sensitizations during early childhood. There is also a striking fall in the percentage of reactions occurring between the eighth and twelfth year periods. This is in agreement with the recognized tendency for asthma to be gradually outgrown in late childhood. We have long been aware that most of the asthmatic children failing to give any skin reactions are found in the later years of childhood. This must be true if there is a falling off in the percentage of both food and inhalant reactions.

Returning to a consideration of the rising incidence of inhalant sensitizations between the years of 2 and 8, and the inference that hypersensitiveness to inhalant proteins is most commonly an acquired state, let us review a few cases for detailed evidence. Similar cases

encountered among adults have previously been reported by Rackemann.[2] An infant (I. B.) was seen at 8 months because of eczema, and was found to give tremendous reactions to egg, beef and milk, but was entirely negative to all inhalants including cat hair. This child was successfully treated for her food idiosyncrasies and her eczema gradually disappeared; she returned at the age of 3½ years because of three severe asthmatic attacks during the preceding few months. At this time she was negative to all the food proteins, but gave a strong reaction to cat hair. With the exception of two occasions following unavoidable contact with cats, she kept free from symptoms until last seen about two years later, at which time the reaction to cat hair was still present Admitting that a single negative scratch test to cat hair is not absolute proof that sensitization was not present in infancy, yet the whole picture strongly suggests the development of this reaction between the ages of 1 and 3 years.

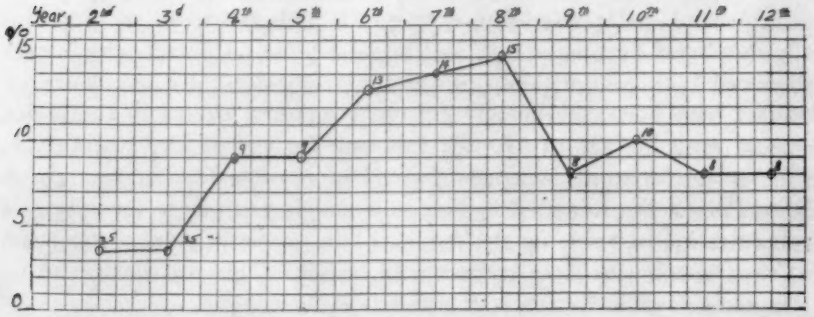

Chart 2.—Distribution of cases of hypersensitiveness to inhalant proteins according to age. Based on eighty-seven positive cases.

Another subject (F. McQ.) tested to dog hair in 1921 and found negative, acquired a dog for a house pet in 1923. For the first few months no untoward results were noted, but gradually the boy's asthma became aggravated, and he was brought to us with the specific request that he be tested with dog hair. The test proved to be strongly positive, and removal of the dog gave great relief. There are numerous other cases in the series that could be cited, but space will only permit the mention of one other boy found to react strongly to mustard on the first test. A history was obtained that his mother had been in the habit of rubbing his chest with mustard paste to relieve dyspnea in attacks, but after two or three years he began to develop hives when the mustard was applied and his asthma was aggravated by it.

2. Rackemann, K. F. M.: Can Hypersensitiveness be Acquired? J. A. M. A. **84**:489 (Feb. 14) 1925.

COMMENT

It would be futile to discuss the question as to whether these are really changes from absence to presence of hypersensitiveness and vice versa, or simply differences in degree above or below the reactive level. To assume that an allergic person is born hypersensitive to every known protein, but that only a few are at any time above the threshold of reactivity, is simply considering that person fundamentally different from the normal. This difference is admitted, but we only use the term hypersensitive when either clinically or by test an abnormal reaction can be elicited. In this sense, surely, states of hypersensitiveness are both developed and overcome during short spans of childhood.

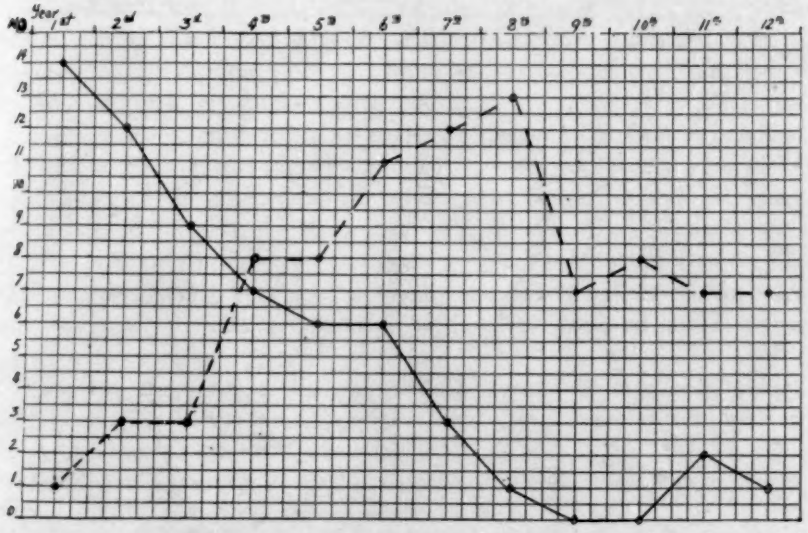

Chart 3.—Number of cases found hypersensitive to food and inhalants per year of age. Food cases, straight line; inhalant cases, broken line.

It is not our purpose to draw any conclusions regarding fundamental differences between food and inhalant sensitizations, for the difference is probably dependent on rather superficial questions of contact, dosage, etc. But attention has been called to these facts for the practical reason that they must be kept in mind when treating children. A child should not for long be considered as a subject sensitive to horse dander or to egg white, but as a complex of changing and multiple sensitizations. At this age, it is imperative to retest at frequent intervals, preferably every six months, those who are not remaining free from symptoms.

By referring to chart 3, which gives the number of cases of food and inhalant sensitizations, separately graphed as to number of cases occurring each year, we get the general expectancy in this changing

course. First, two or three years with foods as the primary factors of importance, then a similar period with about an equal division between foods and inhalants, with most cases showing both types of sensitization. Finally, a period of years with inhalant reactions very commonly found and practically the only protein factors, but with an increasing number of cases failing to show any protein sensitizations.

Chart 4 is based only on those cases completely tested to both groups of proteins, and shows the percentage division between the two groups in each of the year periods. This chart shows the age characteristics even more strikingly.

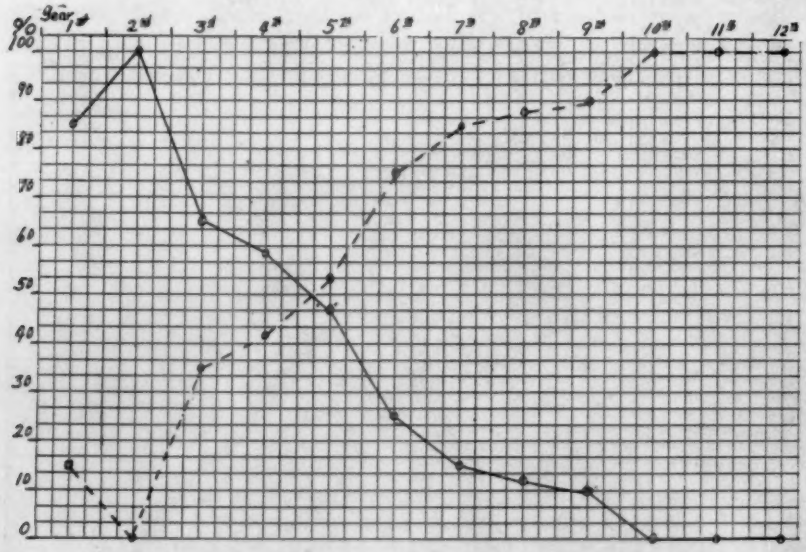

Chart 4.—Percentage division between food and inhalant sensitizations per year of age. Based only on children fully studied. Food positives, straight line; inhalant positives, broken line.

One other conclusion might be drawn from these findings. If sensitization to inhalant proteins is frequently acquired during the early years of childhood, it would seem advisable to avoid unnecessary contact with these substances in asthmatic children. Ratner found rabbit hair one of the most common positive reactions among children coming to the Nursery and Child's Hospital in New York, and found rabbit hair the chief element in their bedding.[3] We in Boston rarely encounter rabbit hair as causing reactions, but find goat and hog hair common and cat hair leading. A subject already referred to developed sensitization to dog hair a few months after the acquisition of a dog. The same child

3. Ratner, B.: Rabbit Hair Asthma in Children, Am. J. Dis. Child. **24**:346 (Oct.) 1922.

showed a marked reaction to coyote fur, and his mother's coat proved to be of this material. The case of the laboratory diener who became sensitive to guinea-pig hair is familiar.[4] With so much evidence that close contact with an inhalant protein, in childhood at least, increases the probability that the patient will become hypersensitive to that protein, it would seem to be good judgment to proscribe for an asthmatic child feather pillows, hair mattresses, horseback riding, fur coats and pets of all kinds, regardless of the protein test findings.

SUMMARY AND CONCLUSION

Evidence is presented to confirm the general impression that hypersensitiveness to food proteins is most commonly encountered in early childhood, and that there is a natural loss of sensitivity to these substances during childhood. The age at which such loss will take place, is, however, not predictable. No case could be found showing definitely the development of a specific food idiosyncrasy.

Figures are given showing the rarity of hypersensitiveness to inhalant proteins in infants, and that the number of cases encountered increases rapidly during the middle period of the first decade. Cases are cited which strongly suggest the acquisition of specific inhalant sensitizations.

The inference is drawn that hypersensitivity to food proteins tends to be present at birth and to be gradually lost during childhood, whereas hypersensitivity to inhalant proteins tends to be acquired and is more resistant to change.

There is, therefore, a changing state of sensitization to be expected during childhood, and protein tests should be frequently repeated to obtain the best results with treatment.

Excessive exposure to inhalant proteins which show negative skin tests should be avoided in the asthmatic child.

Active treatment by oral desensitization of subjects found to react to important food substances is preferable to awaiting the natural loss of such hypersensitivity.

4. Rackemann, K. F. M.: M. Clin. N. Am. **7**:765 (Nov.) 1923.

METABOLISM OF UNDERNOURISHED CHILDREN

II. BASAL METABOLISM *

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The first paper in our series of studies of undernourished children described various factors concerned in malnutrition, and gave data concerning the gain in weight when the children were fed in the hospital. The next phase of the subject is that of the basal metabolism of the same underweight children. Our metabolism figures have been referred to the standards published by Benedict and Talbot,[1] but we have determined basal metabolism on normal children besides, so that we might note any variations between our normal children and theirs which might be due to differences in locality or experimental conditions.

Little work has been reported on basal metabolism in malnutrition, and most of it has concerned infants. Blunt and her collaborators [2] worked with older children, and found a high total metabolism calculated on the basis of the Benedict-Talbot weight standards as well as an excess metabolism per kilogram and per square meter of body surface. This is the only work that we know which is comparable with ours.

EXPERIMENTAL

For all of our determinations, Benedict's cot chamber with universal respiration apparatus was used. Alcohol checks given in table 4 were run with every change of acid or soda lime, and all precautions outlined by Benedict were carefully observed. The child was put into the bed early in the morning, without breakfast, and after a preliminary period of thirty minutes duplicate determinations of thirty minutes each were made. One day was given over to training the child to accustom itself

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* The first article of this series appeared in the July issue, Am. J. Dis. Child.

1. Benedict, F. G., and Talbot, F. B.: Metabolism and Growth from Birth to Puberty, Pub. 302, Carnegie Inst. Washington, 1921.

2. Blunt, K.; Nelson, A., and Oleson, H. C.: The Basal Metabolism of Underweight Children, J. Biol. Chem. **49**:247, 1921.

to the machine, and tests were then made on three consecutive days for each set of figures reported; the two lowest figures were used and all the computations were made on the average of the two. Kymograph records of activity were obtained in all experiments, and pulse rate was counted by means of a stethoscope at fifteen minute intervals. In all instances the children were awake, but were kept as quiet as possible.

The report covers the same children discussed in the first paper of the series. In some cases the same child appears in more than one group because his gain in weight while with us was sufficient to bring him to a figure nearer that of normal children. Each time a child is recorded represents a new series of six metabolism determinations. Nine normal girls were obtained; in our tables we have referred to them as vigorous normal girls because they looked well and healthy and were vigorous and active. All the rest, fourteen boys and eighteen girls, were sent to us as underweight children, but some of them gained weight so rapidly when on diet that they were nearly normal when their metabolism was taken. We have put these into a second group, which we have called normal in weight but not vigorous. Most of the members of this group had just reached normal weight. The groups are arbitrarily divided into these two sets of normals, then as 5.1 to 10.0 per cent underweight, 10.1 to 15.0 per cent underweight, and more than 15 per cent underweight. In all, fifty-two sets of basal metabolism determinations are recorded on these forty-one children. One girl who appeared in the prevous paper has been omitted from this one because she slept during all the metabolism tests. Some records have been obtained on children asleep and awake which we shall report on in a later paper.

COMMENT

A summary of our findings appears in table 1. On using Baldwin's standards [3] for height, we were struck by the fact that nearly all of our children were somewhat under height, and more than a third of them were 5 per cent or more below the standard. Since Baldwin's children were chiefly American children in Iowa or children of the taller European races, we compared our children with the standards worked out by Boas [4] on city children, and found much less variation. Following this standard, only four of our subjects are more than 5 per cent below average height for children of more diverse stock and large city environment, and many of them, in fact, are slightly above the average. For this reason we are not inclined to attempt any conclusions concerning

3. Baldwin, B. T.: The Physical Growth of Children from Birth to Maturity, University of Iowa, **2**:1541, 1921.

4. Boas, F.: Report U. S. Comm. Ed. 1896-1897.

TABLE 1.—*Summary of Basal Metabolism Data on Normal and Undernourished Children*

Subject	Age	Sex*	Height: Found, Cm.	Height: Variation from Average: Baldwin Standard, per Cent	Height: Variation from Average: Boas Standard, per Cent	Stem Length, Cm.	Weight: Found, Kg.	Weight: Variation from Average, per Cent	Heat Production: Test I per 24 Hours, Calories	Heat Production: Test II per 24 Hours, Calories	Heat Production: Average: Per 24 Hours, Calories	Heat Production: Average: Per Kilogram, Calories	Heat Production: Average: Variation from Normal: Ref. to Age, per Cent	Heat Production: Average: Variation from Normal: Ref. to Weight, per Cent	Heat Production: Average: Variation from Normal: Ref. to Height, per Cent	Pulse Rate	Respiratory Quotient	Activity
Vigorous Normals																		
R. W.	11	♀	140	−1.4	+2.2	75	34.6	+5.8	1,280	1,290	1,285	37	+28.5	+ 9.8	+20.4	72	0.84	−
M. H.	9	♀	123	−6.8	−2.4	64	23.9	+3.2	1,047	1,051	1,049	44	+13.4	+16.7	+17.4	90	0.80	−
A. G.	5	♀	108	+0.9	+2.9	59	18.1	+1.7	987†	.....	987	55	+31.6	+29.9	+31.8	84	0.82	+
H. P.	4	♀	105	+6.1	+6.1	58	16.6	+0.6	793†	.....	793	48	+13.3	+ 9.4	+10.1	86	0.84	−
F. J.	10	♀	132	−3.6	+0.8	71	27.5	−2.5	1,125	1,130	1,127	41	+16.2	+13.6	+14.5	78	0.83	+
B. L.	11	♀	138	−2.8	+0.7	73	30.9	−2.8	1,067	1,067	1,067	35	+ 6.7	− 0.7	+ 1.9	84	0.81	+
S. W.	8	♀	118	−7.1	−2.5	64	20.9	−3.2	820	825	823	39	− 5.7	− 1.7	− 3.2	80	0.82	−
H. S.	9	♀	132	±0.0	+4.5	70	27.2	−3.5	992	1,000	996	37	+ 7.7	+ 2.2	+ 1.1	84	0.81	−
R. G.	10	♀	133	−2.9	+1.5	70	27.5	−4.5	980	980	980	36	+ 1.0	− 1.0	− 1.5	76	0.82	−
Average													+12.5	+ 8.7	+10.3			
Normal in Weight, but Not Vigorous																		
R. M.	5	♂	95	−11.2	−10.4	53	14.5	+0.7	876	888	882	60	+11.6	+24.2	+18.4	..	0.83	+
E. G.	6	♀	109	−4.4	−0.9	60	18.1	−0.5	972	980	976	54	+22.0	+29.3	+28.6	86	0.81	+
N. G.	7	♂	106	−13.1	−9.4	58	16.8	−1.8	862	.....	862	51	− 4.2	+11.2	+ 6.4	84	0.79	−
E. B.	5	♀	105	−1.9	±0.0	58	16.4	−1.9	853	854	853	52	+13.7	+18.2	+18.5	82	0.85	+
H. D.	5	♂	93	−13.1	−12.3	53	13.5	−2.9	788	816	802	59	+ 1.5	+17.9	+ 9.9	100	0.87	−
I. Ba.	10	♂	140	+2.2	+6.1	74	30.8	−3.1	1,128	1,158	1,143	37	+ 6.3	+ 0.3	− 1.9	78	0.85	+
J. R.	4	♀	104	+5.1	+5.1	57	15.7	−4.3	742	742	742	47	+ 6.0	+ 6.0	+ 4.4	98	0.85	++
R. G.	6	♂	108	−7.7	−3.6	59	16.9	−4.5	999	999	999	59	+19.7	+28.1	+21.8	82	0.84	++
E. G.	6	♀	108	−5.3	−1.8	59	17.0	−4.5	953	984	984	56	+19.1	+28.8	+27.4	84	0.81	−
J. G.	8	♂	124	−2.4	+1.6	64	22.6	−5.0	1,122	1,124	1,123	50	+17.0	+21.4	+24.2	90	0.83	+
G. L.	13	♀	142	−6.6	−4.7	73	34.1	−5.0	1,179	1,185	1,182	35	+ 7.4	+ 4.6	+ 8.5	84	0.81	+
Average													+10.9	+17.3	+15.1			

5.1% to 10% Underweight																	
E. D.	10	♂	131	−4.4	−0.8	71	25.7	−5.5	1,016	1,016	1,016	40	− 5.5	+ 0.6	− 4.2	68	0.85	−
J. G.	8	♂	123	−3.2	−0.8	67	22.1	−5.9	1,120	1,114	1,117	51	+16.4	+21.4	+15.8	92	0.84	+
A. Go.	10	♀	134	−2.2	+2.3	72	27.5	−6.5	1,010	1,012	1,011	37	+ 4.2	+ 2.4	+ 0.6	82	0.82	−
B. G.	9	♀	121	−8.3	−4.0	66	20.5	−6.7	927	948	938	46	+ 1.4	+14.7	+ 7.2	84	0.86	+
R. G.	6	♂	108	−7.7	−3.6	60	16.4	−7.3	906	906	906	59	+15.7	+25.8	+17.8	88	0.85	++
T. F.	10	♂	128	−6.6	−3.0	69	24.0	−7.9	1,121	1,114	1,118	47	+ 4.0	+15.3	+ 9.1	88	0.84	+
M. Da.	4	♀	98	−1.1	−1.1	55	13.5	−8.2	749	749	749	55	+ 7.0	+15.2	+13.6	82	0.81	+
L. C.	6	♀	115	+0.9	+4.5	64	18.5	−8.9	868	868	868	47	+ 8.5	+12.7	+ 5.8	100	0.85	−
M. S.	9	♀	125	−5.3	−0.8	68	21.9	−9.1	1,031	1,028	1,030	47	+11.3	+21.2	+12.6	104	0.83	+
A. Go.	10	♀	134	−2.2	+2.3	72	26.6	−9.5	1,082	1,081	1,082	41	+11.6	+12.7	+ 7.7	88	0.79	−
S. K.	10	♂	137	±0.0	+3.8	74	27.6	−9.5	1,055	.....	1,055	38	− 1.9	− 0.5	− 6.6	78	0.79	−
A. B.	6	♀	117	+2.6	+6.4	64	18.9	−9.6	897	881	889	47	+11.1	+14.7	+ 6.2	88	0.80	+
H. L.	8	♀	118	−7.1	+2.5	64	19.5	−9.7	1,049	1,045	1,047	54	+20.4	+32.0	+23.6	100	0.82	++
C. S.	10	♂	136	−0.7	+3.0	73	26.9	−9.7	1,227	1,216	1,221	45	+13.6	+16.2	+ 9.5	82	0.82	+
J. M.	13	♂	138	−9.2	−5.5	74	28.2	−9.9	1,260	1,236	1,248	44	− 0.1	+16.6	+ 9.5	76	0.83	+
Average													+ 7.8	+14.7	+ 8.5			
10.1% to 15% Underweight																		
N. G.	7	♂	106	−13.1	−9.4	58	15.3	−10.5	1,059	1,046	1,052	69	+16.9‡	+42.1‡	+29.8‡	86	0.79	++
L. C.	6	♀	115	+0.9	+4.5	63	18.0	−11.3	908	906	904	50	+13.0	+19.7	+10.6	94	0.86	+
M. M.	7	♂	116	−4.9	−0.9	63	17.9	−11.8	862	847	855	48	− 5.0	+ 6.2	− 3.4	86	0.79	+
B. G.	8	♀	120	−5.5	−0.8	65	19.4	−12.2	972	989	980	50	+12.2	+22.9	+13.2	94	0.81	++
M. Do.	7	♀	120	+0.8	+3.5	65	19.1	−13.6	952	948	950	50	+13.1	+21.8	+ 9.7	98	0.83	++
H. G.	11	♂	138	−2.8	+1.5	74	26.5	−13.9	1,077	1,090	1,083	41	− 3.7	4.6	− 5.0	96	0.79	−
L. A.	10	♀	129	−5.8	−1.5	70	22.8	−13.9	1,030	1,027	1,029	45	+ 6.1	+17.6	+ 7.5	78	0.83	+
L. C.	6	♀	115	+0.9	+4.5	63	17.2	−14.0	928	934	931	54	+16.4	+25.8	+13.9	94	0.85	−
A. B.	6	♀	116	+1.8	+5.5	63	17.0	−14.8	880	885	882	52	+10.2	+20.0	+ 6.5	86	0.80	+
Average													+ 7.8	+16.1	+ 6.6			
More Than 15.1% Underweight																		
D. Y.	7	♀	116	−2.5	±0.0	63	17.3	−16.0	958	958	956	55	+13.8	+29.2	+15.4	94	0.83	+
S. K.	10	♂	137	±0.0	+3.8	74	25.6	−16.1	1,082	1,089	1,086	42	+ 1.0	+ 8.1	− 3.9	80	0.79	−
R. B.	6	♂	112	−4.3	±0.0	61	15.6	−18.3	994	992	993	64	+18.9	+34.2	+16.8	92	0.78	+
A. Go.	10	♀	133	−2.9	+1.5	72	23.0	−20.0	1,012	1,014	1,013	44	+ 4.4	+15.1	+ 1.8	88	0.80	+
L. P.	8	♀	132	+3.1	+9.1	71	22.4	−20.6	1,008	1,005	1,004	45	+15.4	+15.4	+ 1.9	86	0.83	+
R. N.	11	♀	141	−0.7	+2.9	76	25.3	−24.3	1,115	1,117	1,116	44	+11.6	+19.3	+ 3.4	..	0.83	++
A. Go.	8	♀	125	−1.6	+3.3	68	18.0	−25.3	775	793	784	44	− 9.9	+ 3.0	−16.7	88	0.77	−
A. Go.	10	♀	132	−3.6	+0.8	71	20.9	−25.9	922	920	921	44	− 5.0	+10.9	− 6.5	92	0.81	−
Average													+ 6.3	+16.9	+ 1.5			

* In this column, ♀ indicates female; ♂, male.
† Child slept during all the other tests.
‡ Not included in average (see discussion).

either the prevalence of short or tall children among the undernourished, or the basal metabolic rate in relation to variation from normal height.

Actual values for the basal metabolism of each child are given in the table, but for purposes of comparison we have figured the percentage variation from normal metabolism predicted by Benedict and Talbot for age, weight and height. In this way we can make comparisons not so much affected by the factors of age and sex. The metabolism per unit of surface area was also computed and referred to standards for age and weight. In most cases the variations from standards were slightly higher than those of the total twenty-four hour metabolism. To save space we have not tabulated these figures in this paper.

We find that our vigorous normal children show an average basal metabolism about 10 per cent higher than the standards reported by Benedict. It has been before noted that all of our children were awake during the experiments. Benedict gives no figures to show the prevalence of wakefulness in the children in his series, but intimates, at least, that many of them were asleep. While figures for sleeping children are perhaps more desirable, laboratory conditions are often such that it is impossible to obtain them, and since most investigators will probably find it easier to work with children awake, we have chosen to report only such cases. It is often extremely difficult to keep a young child quiet enough for a strict basal determination throughout a period of one and a half hours. We have, therefore, analyzed our kymograph records for the determinations employed in the table and have divided them into three groups. Kymograph records are here reproduced to show the three classes of activity.

We have had several cases in which basal records were obtained on a sleeping child, and again on the same child awake but with no activity recorded, and while we cannot make definite statements on the basis of our limited data, the indications are that a basal record may be as much as 10 to 15 per cent higher on the waking child than during sleep. On the strength of these findings, we feel that our results may be cut about 10 per cent to make them strictly comparable with Benedict's.

Treating our figures thus, a cursory glance will reveal the fact that they all fall into the normal class, or 10 per cent from the standard. There are several rather interesting points to be made, however. In our group of vigorous normals, composed entirely of girls, there is less variation from the weight standard than from height or age, but the following groups vary less from the age and height standards than from weight. In the fourth group we have omitted one child, N. G., from the average, because the second set of determinations made about two months after the first and appearing in the second group, show him to

have normal metabolism, which could hardly be accounted for simply by the change in weight in the interim. There seems to be a tendency toward lower metabolism with increasing underweight, as shown especially by the age and height standards. On the other hand, according to the weight standard, the underweights diverge in the opposite direction. This seems reasonable, however, when we consider that with

Chart 1.—This shows no activity.

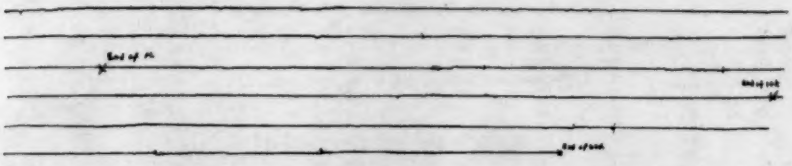

Chart 2.—Some activity.

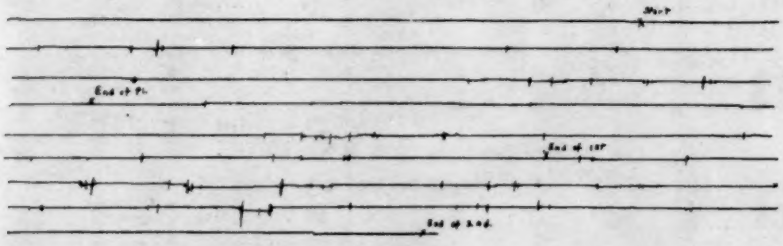

Chart 3.—Activity plus.

increasing underweight there is an increasing proportion of active protoplasmic tissue and a decreasing amount of inert material. Thus, if a child were sufficiently underweight to decrease the amount of active protoplasm besides the fat, the total metabolism would be decreased below that of normal metabolism. But it is seldom that older children show such a degree of emaciation as is found, for instance, in infants. We find that the most underweight children are inclined to be taller than the normal children of corresponding age and their total metabolism is

higher. When compared with the height standard computed by Talbot,[5] however, these children do show a lower total metabolism with increasing underweight.

In table 2 it will be noted that, with the exception of A. G. and M. H., the normal girls show a normal metabolism per kilogram of body weight. In the second group, which includes those who reached normal weight after they came to us, all are high except one boy, I. Ba., and

TABLE 2.—*Per Kilo Metabolism of Normal and Undernourished Children*

Boys				Girls			
Subject	Age	Found	Normal	Subject	Age	Found	Normal
			Vigorous Normals				
				H. P.	4	48	44
				A. G.	5	55	42
				S. W.	8	39	38
				M. H.	9	44	37
				H. S.	9	37	37
				F. J.	10	41	36
				R. G.	10	36	36
				R. W.	11	37	35
				B. L.	11	35	35
			Normal in Weight, but Not Vigorous				
R. M.	5	60	44	J. R.	4	47	44
H. D.	5	59	44	E. B.	5	52	42
R. G.	6	59	43	E. G.	6	54	40
N. G.	7	51	42	E. G.	6	56	40
J. G.	8	50	40	G. L.	13	35	34
I. Ba.	10	37	37				
			5.1 to 10 per cent Underweight				
R. G.	6	59	43	M. Da.	4	55	44
J. G.	8	51	40	L. C.	6	47	40
E. D.	10	40	37	A. B.	6	47	40
T. F.	10	47	37	H. L.	8	54	38
S. K.	10	38	37	B. G.	9	46	37
C. S.	10	45	37	M. S.	9	47	37
J. M.	13	44	32	A. Go.	10	37	36
				A. Go.	10	41	36
			10.1 to 15 per cent Underweight				
N. G.	7	69	42	L. C.	6	50	40
M. M.	7	48	42	L. C.	6	54	40
H. G.	11	41	36	A. B.	6	52	40
				M. Do.	7	50	39
				B. G.	8	50	38
				L. A.	10	45	36
			More Than 15 per cent Underweight				
R. B.	6	64	43	D. Y.	7	55	39
S. K.	10	42	37	L. P.	8	45	38
				A. Go.	8	44	38
				A. Go.	10	44	36
				A. Go.	10	44	36
				R. N.	11	44	35

one girl, G. L. The rest of those underweight show a rather consistently high metabolism per kilogram, with no differentiation as to percentage underweight. This is to be expected from the work of Benedict and Talbot [6] and also that of Blunt. We do not feel that the second group of children can properly be regarded as normal because they came to

5. Talbot, F. B.: Basal Metabolism of Children, Physiol. Rev. **5**:477, 1925.

6. Benedict, F. G., and Talbot, F. B.: Studies in Respiratory Exchange of Infants, Am. J. Dis. Child. **8**:1 (July) 1914.

TABLE 3.—*Relation Between Basal Metabolism and Caloric Intake*

Subject	Age	Sex*	Variation from Normal Weight	Intake per 24 Hours	Basal Metabolic Rate	Gain in Weight	Intake / Basal
Vigorous Normals							
R. W.	11	♀	+5.8	1,775	1,285	2.2	1.4
M. H.	9	♀	+3.2	1,816	1,049	0.0	1.7
A. G.	5	♀	+1.7	1,662	987	3.8	1.7
H. P.	4	♀	+0.6	1,238	798	3.2	1.6
F. J.	10	♀	−2.5	1,781	1,127	1.5	1.6
B. L.	11	♀	−2.8	1,784	1,067	0.0	1.7
S. W.	8	♀	−3.2	1,655	820	4.4	2.0
H. S.	9	♀	−3.5	2,026	996	0.0	2.0
R. G.	10	♀	−4.5	1,777	980	3.0	1.8
Average							1.7
Normal in Weight, but Not Vigorous							
R. M.	5	♂	+0.7	1,354	882	5.4	1.5
E. G.	6	♀	−0.5	1,628	976	1.2	1.7
N. G.	7	♂	−1.8	1,560	862	2.3	1.8
E. B.	5	♀	−1.9	1,674	853	9.0	2.0
H. D.	5	♂	−2.9	1,268	802	4.0	1.6
I. Ba.	10	♂	−3.1	1,722	1,143	0.3	1.5
J. R.	4	♀	−4.3	1,244	742	5.5	1.7
R. G.	6	♂	−4.5	1,704	999	1.3	1.7
E. G.	6	♀	−4.5	1,620	984	1.2	1.6
J. G.	8	♂	−5.0	1,942	1,123	1.4	1.7
G. L.	13	♀	−5.0	2,171	1,182	−0.6	1.8
Average							1.7
5.1 per cent to 10 per cent Underweight							
E. D.	10	♂	−5.5	1,742	1,016	0.8	1.7
J. G.	8	♂	−5.9	1,942	1,117	1.4	1.7
A. Go.	10	♀	−6.5	1,775	1,011	2.2	1.8
B. G.	9	♀	−6.7	1,705	938	0.0	1.8
R. G.	6	♂	−7.3	1,704	966	1.3	1.8
T. F.	10	♂	−7.9	1,854	1,118	1.7	1.7
M. Da.	4	♀	−8.2	.....	749	6.0	...
L. C.	6	♀	−8.9	1,691	868	1.1	1.9
M. S.	9	♀	−9.1	1,591	1,030	2.1	1.5
A. Go.	10	♀	−9.5	1,775	1,082	2.2	1.6
S. K.	10	♂	−9.5	2,307	1,055	1.5	2.2
A. B.	6	♀	−9.6	1,334	889	1.7	1.5
H. L.	8	♀	−9.7	1,514	1,047	1.6	1.4
C. S.	10	♂	−9.7	1,799	1,221	1.9	1.5
J. M.	13	♂	−9.9	2,076	1,248	2.3	1.7
Average							1.7
10.1 per cent to 15 per cent Underweight							
N. G.	7	♂	−10.5	1,673	1,052	2.3	1.6
L. C.	6	♀	−11.3	1,603	904	1.1	1.8
M. M.	7	♂	−11.8	1,615	855	1.1	1.9
B. G.	8	♀	−12.2	2,081	980	2.6	2.1
M. Do.	7	♀	−13.1	1,419	950	1.1	1.5
H. G.	11	♂	−13.9	1,979	1,083	4.8	1.8
L. A.	10	♀	−13.9	.....	1,029	−0.7	...
L. C.	6	♀	−14.0	1,275	931	1.1	1.4
A. B.	6	♀	−14.8	1,394	882	1.7	1.6
Average							1.7
More than 15.1 per cent Underweight							
D. Y.	7	♀	−16.0	1,573	956	0.9	1.6
S. K.	10	♂	−16.1	2,312	1,086	1.5	2.1
R. B.	6	♂	−18.3	1,587	998	7.0	1.6
A. Go.	10	♀	−20.0	1,439	1,013	2.2	1.4
L. P.	8	♀	−20.6	1,633	1,004	0.8	1.6
R. N.	11	♀	−24.3	1,250	1,116	0.9	1.1
A. Go.	8	♀	−25.3	1,189	784	0.9	1.5
A Go.	10	♀	−25.9	1,431	921	2.2	1.6
Average							1.6

*In this column, ♀ indicates female; ♂, male.

us as underweight children, and usually gained weight so fast that perhaps they had not yet become adjusted to a change after maintaining a high level of energy production for a long time. This assumption is strengthened by the fact that I. Ba. and G. L. were the only ones who were normal in weight when they came, and both show normal and total metabolism per kilogram. They were put into this group because they looked pale and were not so active as most normal children are.

TABLE 4.—*Alcohol Checks*

Date	Respiratory Quotient	Respiratory Quotient Average	Date	Respiratory Quotient	Respiratory Quotient Average
9/ 8/23	0.663		11/ 5/24	0.663	
	0.671			0.680	
	0.666	0.666		0.655	0.666
9/ 9/23	0.661		11/10/24	0.658	
	0.681	0.671		0.655	
				0.671	0.661
9/10/23	0.672		11/17/24	0.666	
	0.682			0.660	
	0.662	0.672		0.672	0.666
9/15/23	0.666		11/21/24	0.662	
	0.667	0.667		0.664	0.663
9/18/23	0.664		12/31/24	0.674	
	0.655	0.660		0.671	0.672
9/23/23	0.662		1/ 2/25	0.666	
	0.667			0.668	0.667
	0.668		1/ 9/25	0.673	
	0.663	0.665		0.663	0.668
10/ 1/23	0.667		4/ 4/25	0.670	
	0.661	0.664		0.658	0.664
10/19/23	0.677		4/ 3/25	0.653	
	0.678	0.677		0.666	
10/22/23	0.672			0.671	0.663
	0.668	0.670	4/ 9/25	0.682	
1/18/24	0.657			0.657	
	0.664	0.661		0.670	0.669
4/10/24	0.666		6/ 1/25	0.663	
	0.657	0.661		0.657	0.660
6/21/24	0.679		7/22/25	0.665	
	0.664	0.671		0.665	0.665
10/ 4/24	0.652		8/ 1/25	0.672	
	0.661	0.657		0.662	
10/ 7/24	0.667			0.677	0.670
	0.669		11/14/25	0.671	
	0.669	0.668		0.664	0.668

The pulse rates and respiratory quotients are listed in table 1, and both fall within the limits of the cases reported by Benedict.

Table 3 shows an interesting relationship between basal metabolism and food intake. In all groups the ratio is 1:1.7. The plan was to feed each child the requirement for its age according to Holt,[7] but

7. Holt, L. E.: Food, Health and Growth, New York, The Macmillan Company, 1922.

this could not be adhered to strictly, because some children were not satisfied with that amount, and since one of the objects of the work was to make them gain weight, we naturally allowed them to eat as much as they wished. Others could not even be urged to eat the required amount. Regardless of this, the food intake maintains a very constant average level in respect to the basal metabolism, and this whether the child is gaining slowly, gaining rapidly or not gaining at all. Possibly an increase in caloric intake leads to an increase in basal metabolism. It would be interesting to feed children a high caloric diet for some time and note the effect on the basal metabolism.

SUMMARY

The report covers a study of the basal metabolism of nine normal and thirty-two undernourished children. The division between the two groups is arbitrarily made at more than 5 per cent below average weight.

Most of the children were found to be under average height according to Baldwin, but most of them came up to the average with the Boas standards.

Basal metabolism per unit of body surface was computed, but was not reported because it varied in the same direction as the basal metabolism according to total heat production.

Normal children vary less from the predicted metabolism according to weight than from any other standard. Underweight children, however, adhere more closely to the figures for age and height. All the children are within normal limits, but the basal metabolism seems to decrease with increasing underweight, especially when computed on the basis of height. According to weight, the basal metabolism of underweight children is increased over normal, but shows no relation to degree of underweight.

Normal children show a normal per kilogram metabolism, but that of underweight is high. There seems to be no definite relation between the increase in metabolism per kilogram and the degree of underweight.

Food intake maintains a rather constant level of 1.7 times the caloric value of the basal metabolism.

Kymograph records of activity, pulse rates, and respiratory quotients are reported.

METABOLISM OF UNDERNOURISHED CHILDREN

III. URINARY NITROGEN WITH SPECIAL REFERENCE TO CREATININE *

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Previous papers have dealt with gain in weight [1] and energy metabolism [2] of undernourished children. The current article opens the discussion of the substance metabolism of the same children, and will deal with some of the urinary nitrogenous constituents. Nitrogen balance, mineral metabolism and caloric intake and output will be discussed in papers to follow. Very little material is available on the substance metabolism of undernourished children, since most investigators of the problem of malnutrition have studied infants. Fleming [3] reports no difference in behavior of normal and marantic infants with respect to total urinary, creatinine and ammonia nitrogen, and Utheim [4] finds normal creatinine values, but a high excretion of ammonia nitrogen concurrent with high organic acids which decrease with improvement in the nutritional state of the infant.

EXPERIMENTAL

Most of the subjects used in this work have already been reported for gain in weight and for basal metabolism. For substance metabolism, diets were carefully controlled by a dietitian especially appointed to this work. Twenty-four hour specimens of urine were collected for three-day periods and analyzed for total nitrogen by the Kjeldahl method, and for creatine, creatinine and ammonia nitrogen by Folin's

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1. Wang, C. C.; Frank, M.; Hays, B. B., and Kern, R.: Metabolism of Undernourished Children. 1. Gain in Weight, Am. J. Dis. Child. **32**:63 (July) 1926.

2. Wang, C. C.; Kern, R.; Frank, M., and Hays, B. B.: Metabolism of Undernourished Children. 2. Basal Metabolism, Am. J. Dis. Child., this issue, p. 350.

3. Fleming, G. B., and Hutchinson, H. S.: A study of the Metabolism in the Undernourished Infant, Quart. J. Med. **68**:339, 1924.

4. Utheim, K.: Metabolism Studies in Infants Suffering from Chronic Nutritional Disturbances (Athrepsia), Am. J. Dis. Child. **22**:329 (Oct.) 1921.

methods.[5] Foods were also analyzed for nitrogen by the Kjeldahl method. On the controlled diets the children were given cereal, milk, bread, butter, sugar, carrots, oranges, potatoes, meat and egg. The intake was as nearly as possible what a child of the same age but of expected height and weight would require. Nine boys and seventeen girls are reported for creatinine excretion and fourteen boys and seventeen girls for total and ammonia nitrogen. In all, this represents fourteen boys and twenty-seven girls. Each figure given in the following tables represents the average of duplicate determinations of the three twenty-four hour specimens.

COMMENT

In the discussion on basal metabolism, the children were arbitrarily divided into five groups, the first comprising those who were not only normal in weight but who were robust and active; the second group included those who were normal in weight but otherwise below par, although they showed no pathologic symptoms; and the underweight groups were separated at 10, 15, and more than 15 per cent below average. The same divisions were kept in the tables of this paper, and this accounts for the fact that two of our so-called vigorous normal children are slightly more than 5 per cent underweight, since the diets were run shortly after the admission of the children to the hospital.

The vigorous normal children, together with some underweight children, served as subjects in a series of experiments involving high and low protein intakes, and they are reported in this paper for creatinine only, since the figures for ammonia, creatine and total nitrogen were naturally affected by the change. The blanks in the column for creatinine nitrogen in table 1, therefore, do not indicate that no creatine was found. All of the children whom we have used as subjects have shown creatinuria, and indications are that this condition is a covariant with the protein intake. More conclusive figures on this point will be given in the report of the work on high and low protein intakes mentioned in the foregoing.

Table 1 shows that the creatinine coefficients of our normal and underweight children range from 5.5 to 9.5, and do not vary greatly in the various groups. There is a tendency, however, for the average figures to rise until the 10 per cent group is passed, and then to show a slight drop again. It is quite possible that this may be explained by the same assumption that we have made in the report of basal

5. Folin, Otto: On The Determination of Creatinine and Creatine in Urine, J. Biol. Chem. **17**:469, 1914; Folin, Otto; and Bell, Richard: The Colorimetric Determination of Ammonia in Urine, J. Biol. Chem. **29**:329, 1917.

TABLE 1.—*Creatine and Creatinine Nitrogen in Relation to Percentage Underweight*

Date	Subject	Age	Sex*	Weight		Creatine N.		Creatinine N.		
				Kg.	Variation from Normal, per Cent	Per 24 Hours, Mg.	Per Kg. per 24 Hours, Mg.	Per 24 Hours. Mg.	Per Kg. per 24 Hours, Mg.	Creatine N. / Total N. Output
Vigorous Normals										
8/14/25	R. W.	11	♀	35.3	+8.0	..	...	222	6.3	1.5
8/ 7/25	R. W.	11	♀	34.7	+6.1	..	...	211	6.0	1.1
7/17/24	M. H.	9	♀	23.8	+2.6	62	2.5	203	8.5	0.6
6/24/25	A. Ge.	5	♀	17.9	+0.6	..	...	117	6.5	1.5
5/26/25	H. P.	4	♀	17.4	+0.6	..	...	110	6.3	1.6
6/17/25	A. Ge.	5	♀	17.1	−1.2	..	...	110	6.4	2.0
8/13/25	S. W.	8	♀	21.9	−1.4	..	...	165	7.6	1.3
8/28/25	B. L.	11	♀	31.3	−1.6	..	...	238	7.6	1.6
8/28/25	F. J.	10	♀	27.5	−2.5	..	...	210	7.6	1.6
8/ 7/25	S.W.	8	♀	21.0	−2.8	..	...	162	7.7	1.0
9/ 4/25	B. L.	11	♀	30.9	−2.8	..	...	242	7.8	1.2
5/19/25	H. P.	4	♀	16.5	−2.9	..	...	102	6.2	1.6
8/28/25	R. Gl.	10	♀	27.9	−3.1	..	...	192	6.8	1.1
8/21/25	F. J.	10	♀	26.9	−4.6	..	...	198	7.4	1.1
7/18/24	H. S.	9	♀	20.7	−5.3	67	2.4	220	8.6	0.6
8/21/25	R. Gl.	10	♀	27.1	−5.9	..	...	189	7.0	0.8
Average									7.1	
Normal in Weight Only										
2/21/24	R. M.	5	♂	14.4	±0.0	24	1.7	108	7.1	0.4
3/ 5/25	J. G.	8	♂	23.8	±0.0	..	...	170	7.1	1.2
12/19/24	E. G.	6	♀	18.1	−1.1	67	3.7	126	7.0	1.0
2/27/25	R. G.	6	♂	17.5	−1.1	..	...	124	7.1	...
9/11/24	N. G.	7	♂	16.9	−1.2	91	5.4	138	8.2	1.2
2/27/25	J. G.	8	♂	23.5	−1.3	..	...	157	6.7	...
8/22/24	N. G.	7	♂	16.5	−3.5	77	4.6	131	7.9	1.0
12/ 4/24	E. G.	6	♀	17.5	−3.8	47	2.7	118	6.7	0.7
Average									7.4	
5.1 to 10 per cent Underweight										
1/29/25	J. G.	8	♂	22.4	−5.9	112	5.1	180	8.0	1.3
8/14/25	A. Go.	10	♀	27.6	−6.1	..	...	224	8.0	1.5
8/21/25	A. Go.	10	♀	27.5	−6.5	..	...	195	7.1	1.7
12/18/24	L. C.	6	♀	18.7	−7.9	58	3.0	137	7.3	0.8
1/30/25	R. G.	6	♂	16.3	−7.9	73	4.5	118	7.2	1.2
3/ 8/24	E. D.	10	♀	25.0	−8.1	62	2.4	160	6.4	0.8
10/17/24	E. G.	6	♀	16.3	−8.4	89	5.1	136	8.3	1.1
12/ 4/24	L. C.	6	♀	18.4	−9.4	70	3.8	128	6.9	1.0
5/22/24	T. F.	10	♂	23.4	−9.8	73	3.0	199	8.5	0.7
9/11/24	S. K.	10	♂	27.5	−9.8	92	3.3	256	9.3	0.8
Average									7.7	
10.1 to 15 per cent Underweight										
2/21/24	M. S.	9	♀	21.6	−10.4	19	0.9	186	8.6	0.3
9/ 3/25	A. B.	6	♀	18.6	−11.0	..	...	117	6.2	2.1
11/ 6/24	L. C.	6	♀	18.0	−11.3	80	4.5	144	8.0	1.2
4/10/24	M. M.	7	♀	17.9	−11.8	69	3.8	136	7.6	0.9
3/ 7/24	B. B.	5	♀	12.0	−11.8	49	4.1	66	5.5	0.9
8/21/24	S. K.	10	♂	26.8	−12.1	73	2.7	255	9.5	0.5
4/10/24	J. M.	13	♂	27.5	−12.1	59	2.1	235	8.6	0.6
7/31/24	N. G.	7	♂	15.0	−12.3	72	4.8	135	9.0	0.9
Average									7.9	
More than 15 per cent Underweight										
10/17/24	L. C.	6	♀	17.1	−15.8	95	5.5	142	8.3	1.3
5/15/24	D. Y.	7	♀	17.3	−16.0	61	3.5	138	8.0	0.8
3/26/25	M. Do.	7	♀	18.5	−16.3	..	...	133	7.2	1.4
7/31/24	S. K.	10	♂	25.4	−16.7	43	1.7	228	9.0	0.4
7/ 2/25	A. B.	6	♀	16.9	−18.0	..	...	101	6.0	1.4
6/24/25	A. B.	6	♀	16.4	−20.4	..	...	101	6.1	1.5
3/26/25	A. Go.	10	♀	20.1	−23.3	..	...	147	7.3	1.8
4/ 2/25	A. Go.	10	♀	20.6	−23.4	..	...	162	7.9	1.4
5/19/25	A. Go.	10	♀	22.0	−23.6	..	...	164	7.5	1.7
5/26/25	A. Go.	10	♀	22.8	−26.3	..	...	167	7.3	1.4
Average									7.5	

* In this column, ♀ indicates female; ♂, male.

metabolism, namely, that up to 15 per cent underweight the child is simply deficient in the store of body fat and has as much active protoplasmic tissue as the normal child of his height and weight. In this case he would excrete the same amount of creatinine nitrogen, but the amount per kilogram of body weight would be increased.

TABLE 2.—*Creatinine Nitrogen in Relation to Body Weight*

Subject	Age	Sex*	Weight		Creatinine Nitrogen per 24 Hours, Mg.
			Kg.	Variation from Normal	
B. B.	5	♀	12.0	−11.8	66
R. M.	5	♂	14.4	± 0.0	103
N. G.	7	♂	15.0	−12.3	135
R. G.	6	♂	16.3	− 7.9	118
E. G.	6	♀	16.3	− 8.4	136
A. B.	6	♀	16.4	−20.4	101
H. P.	4	♀	16.5	− 2.9	102
N. G.	7	♂	16.5	− 3.5	131
N. G.	7	♂	16.9	− 1.2	138
A. B.	6	♀	16.9	−18.0	101
A. Ge.	5	♀	17.1	− 1.2	110
L. C.	6	♀	17.1	−15.8	142
D. Y.	7	♀	17.3	−16.0	138
H. P.	4	♀	17.4	+ 0.6	110
R. G.	6	♂	17.5	− 1.1	124
E. G.	6	♀	17.5	− 3.8	118
A. Ge.	5	♀	17.9	+ 0.6	117
M. M.	7	♀	17.9	−11.8	136
L. C.	6	♀	18.0	−11.3	144
E. G.	6	♀	18.1	− 1.1	126
L. C.	6	♀	18.4	− 9.4	128
M. Do.	7	♀	18.5	−16.3	133
A. B.	6	♀	18.6	−11.0	117
L. C.	6	♀	18.7	− 7.9	137
A. Go.	10	♀	20.1	−23.3	147
A. Go.	10	♀	20.6	−23.4	162
S. W.	8	♀	21.0	− 2.8	162
M. S.	9	♀	21.6	−10.4	186
S. W.	8	♀	21.9	− 1.4	165
A. Go.	10	♀	22.0	−23.6	164
J. G.	8	♂	22.4	− 5.9	180
A. Go.	10	♀	22.8	−26.3	167
T. F.	10	♂	23.4	− 9.8	199
J. G.	8	♂	23.5	− 1.3	157
J. G.	8	♂	23.8	± 0.0	170
M. H.	9	♀	23.8	+ 2.6	203
E. D.	10	♂	25.0	− 8.1	160
S. K.	10	♂	25.4	−16.7	228
H. S.	9	♀	26.7	− 5.3	229
S. K.	10	♀	26.8	−12.1	255
F. J.	10	♀	26.9	− 4.6	198
R. Gl.	10	♀	27.1	− 5.9	189
A. Go.	10	♀	27.5	− 6.5	195
F. J.	10	♀	27.5	− 2.5	210
J. M.	13	♂	27.5	−12.1	235
S. K.	10	♀	27.5	− 9.8	256
A. Go.	10	♀	27.6	− 6.1	224
R. Gl.	10	♀	27.9	− 3.1	192
B. L.	11	♀	30.9	− 2.8	242
B. L.	11	♀	31.3	− 1.6	238
R. W.	11	♀	34.7	+ 6.1	211
R. W.	11	♀	35.3	+ 8.0	222

* In this column, ♀ indicates female; ♂, male.

When a child is more than 15 per cent below average, however, he begins to show signs of loss of active protoplasm in a lowered basal metabolism and a lowered creatinine coefficient. It seems, therefore, to be more appropriate to use 15 per cent underweight as the margin of undernourishment in children rather than the present figure, 10 per

cent. So far as our figures go, however, we cannot assume that the difference is very marked up to 25 per cent below average, but children more underweight than this are rather difficult to obtain in the present day of school inspection and health programs. When the children were on diet at different times, the creatinine coefficient remained very constant from time to time. The low figure of 5.5 appears in a girl, aged 5 years,

TABLE 3.—*Creatinine Coefficients in Relation to Age and Sex*

Girls					Boys				
Subject	Percentage Variation from Normal Weight	Age	Creatinine Coefficient	Creatinine Nitrogen per 24 Hours	Subject	Percentage Variation from Normal Weight	Age	Creatinine Coefficient	Creatinine Nitrogen per 24 Hours
H. P.	+ 0.6	4	6.3	110					
H. P.	— 2.9	4	6.2	102					
A. Ge.	+ 0.6	5	6.5	117	R. M.	± 0.0	5	7.1	108
A. Ge.	— 1.2	5	6.4	110					
B. B.	—11.8	5	5.5	66					
E. G.	— 1.1	6	7.0	123	R. B.	— 1.1	6	7.1	124
E. G.	— 3.8	6	6.7	118	R. G.	— 7.9	6	7.2	118
L. C.	— 7.9	6	7.3	137					
E. G.	— 8.4	6	8.3	136					
L. C.	— 9.4	6	6.9	128					
A. B.	—11.0	6	6.2	117					
L. C.	—11.3	6	8.0	144					
L. C.	—15.8	6	8.3	142					
A. B.	—18.0	6	6.0	101					
A. B.	—20.4	6	6.1	101					
D. Y.	—16.0	7	8.0	138	N. G.	— 1.2	7	8.2	138
M. Do.	—16.3	7	7.2	133	N. G.	— 3.5	7	7.9	131
					M. M.	—11.8	7	7.6	136
					N. G.	—12.3	7	9.0	135
S. W.	— 1.4	8	7.6	165	J. G.	± 0.0	8	7.1	170
S. W.	— 1.4	8	7.7	162	J. G.	— 1.3	8	6.7	157
					J. G.	— 5.9	8	8.0	180
M. H.	+ 2.6	9	8.5	206					
H. S.	— 5.3	9	8.6	229					
M. S.	—10.4	9	8.6	186					
F. J.	— 2.5	10	7.6	210	E. D.	— 8.1	10	6.4	160
R. Gl.	— 3.1	10	6.8	192	T. F.	— 9.8	10	8.5	199
F. J.	— 4.6	10	7.4	198	S. K.	— 9.8	10	9.3	256
R. Gl.	— 5.9	10	7.0	180	S. K.	—12.1	10	9.5	235
A. Go.	— 6.1	10	8.0	224	S. K.	—16.7	10	9.0	228
A. Go.	— 6.5	10	7.1	195					
A. Go.	—23.3	10	7.3	147					
A. Go.	—23.4	10	7.9	162					
A. Go.	—23.6	10	7.5	164					
A. Go.	—26.3	10	7.3	167					
R. W.	+ 8.0	11	6.3	222					
R. W.	+ 6.1	11	6.0	211					
B. L.	— 1.6	11	7.6	238					
B. L.	— 2.8	11	7.8	242	J. M.	—12.1	13	8.6	235

in the fourth group, but this child was unusually quiet and inactive; in fact, she always went to sleep during the metabolism determination, and showed a low basal value.

There is a definite trend in table 2, showing an increase in twenty-four hour creatinine nitrogen with an increase in body weight, affected very slightly by age except as weight naturally increases with age. For example, H. P., a girl, aged 4 years, has the same creatinine nitrogen

excretion as A. B. who is two years older but weighs approximately the same amount. The same condition may be observed in E. G., aged 6, and A. Ge., aged 5, and twice in A. Go., aged 10, and S. W., aged 8. Among boys and girls of the same weight, boys usually show a somewhat higher creatinine excretion than girls. Both boys and girls increase their creatinine excretion with age, as shown in table 3. The figures would probably be smoother and more conclusive if the number of cases in each group were greater, but we are inclined to the opinion that the increase with body weight is more consistent than the increase with age. Since the two go hand in hand, they must vary in the same direction. There is some divergence of the figures in the 10 and 11 year age groups of girls, but in the 10 year group four of the figures are from one child in the lowest weight group, in which the figures are probably somewhat depressed, and the rest are normal. In the 11 year group, all are normal or above normal. The increase in creatinine excretion with weight could not, of course, be expected to hold in cases in which the body is simply storing fat. The figures for creatinine nitrogen per twenty-four hours show the general upward trend even better than the coefficients.

With one exception (M.H.), all the children in the normal group in table 4 were admitted to the hospital as undernourished children. They gained in weight fairly rapidly, and at the time of experiment their weight had already reached the normal standard. They were, however, far from being healthy in their action and appearance. This fact may account for the lack of difference in the nitrogen output, especially ammonia, in the different groups of children of table 4.

SUMMARY

The creatinine coefficients of twenty-six normal and underweight children ranged from 5.5 to 9.5, with averages of 7.1, 7.4, 7.7, 7.9 and 7.5 for vigorous normal children, normal in weight, 5.1 to 10.0 per cent underweight, 10.1 to 15.0 per cent underweight, and more than 15.0 per cent underweight, respectively. These children showed no signs of diminished creatinine excretion up to 15 per cent below normal weight. Creatinine excretion remained very constant for the same child from time to time.

Creatinine nitrogen increased with increasing body weight and likewise with age, although the latter factor may be secondary to the former.

Creatine occurred in all children examined, and indications are that it varies according to protein intake.

Total and ammonia nitrogen in the urine were approximately the same in all groups.

TABLE 4.—*Total and Ammonia Nitrogen in Relation to Percentage Underweight*

Date	Subject	Age	Sex*	Weight		Nitrogen Intake		Nitrogen Output		Ammonia Nitrogen		
					Variation from Average, per Cent	Per 24 Hrs., Gm	Per Kg. per 24 Hrs., Gm.	Per 24 Hrs., Gm.	Per Kg. per 24 Hrs., Gm.	Per 24 Hrs., Mg.	Per Kg. per 24 Hrs., Mg.	Percentage of Total Nitrogen
				Kg.								
Normal in Weight												
7/17/24	M. H. †.....	9	♀	23.8	+2.6	10.33‡	0.43	9.93	0.42	323	13.6	3.3
2/21/24	R. M.	5	♂	14.4	±0.0	7.23	0.50	5.72	0.40	290	20.8	5.2
11/23/23	H. D.	5	♂	13.8	±0.0	6.86	0.50	4.88	0.35	133	9.6	2.7
12/19/24	E. G.	6	♀	18.1	−1.1	8.91	0.49	6.82	0.38	224	12.3	3.3
9/11/24	N. G.	7	♂	16.9	−1.2	9.78‡	0.58	7.49	0.44	274	16.2	3.7
11/ 6/24	E. G.	6	♀	17.5	−1.7	9.41	0.54	7.72	0.44	261	14.9	3.4
8/22/24	N. G.	7	♂	16.5	−3.5	9.49‡	0.58	8.00	0.48	311	18.8	3.9
12/ 4/24	E. G.	6	♀	17.5	−3.8	8.90	0.51	6.45	0.37	265	15.1	4.1
Average.....							0.52		0.41		15.2	3.7
5.1 to 10 per cent Below Average												
7/18/24	H. S. ‡.....	9	♀	26.7	−5.3	11.80‡	0.44	10.69	0.40	394	14.8	3.7
10/11/23	E. B.	5	♀	15.8	−5.4	8.89	0.56	5.28	0.33	266	16.8	5.0
1/29/25	J. G.	8	♂	22.4	−5.9	9.19	0.41	8.69	0.39	394	17.6	4.5
12/18/24	L. C.	6	♀	18.7	−7.9	9.31	0.50	6.75	0.36	320	17.1	4.7
1/30/25	R. G.	6	♂	16.3	−7.9	8.35	0.51	6.40	0.39	296	18.1	4.6
3/ 8/24	E. D.	10	♂	25.0	−8.1	10.23‡	0.41	8.09	0.32	...	....	...
10/17/24	E. G.	6	♀	16.3	−8.4	7.00	0.43	7.51	0.46	273	16.7	3.6
1/17/24	B. G.	9	♀	20.5	−8.5	9.53‡	0.46	6.66	0.32	362	17.7	5.4
10/25/23	J. R.	4	♀	15.0	−8.5	8.48	0.57	5.47	0.36	225	15.0	4.1
12/ 4/24	L. C.	6	♀	18.4	−9.4	9.14	0.50	7.24	0.39	339	18.4	4.7
2/ 7/24	C. S.	10	♂	27.0	−9.4	9.94	0.37	5.80	0.21	260	9.6	4.5
5/22/24	T. F.	10	♂	23.4	−9.8	10.69‡	0.46	9.64	0.41	389	16.6	4.0
9/11/24	S. K.	10	♂	27.5	−9 8	14.52‡	0.53	11.69	0.43	362	13.2	3.1
Average.....							0.47		0.37		16.0	4.3
10.1 to 15 per cent Below Average												
2/21/24	M. S.	9	♀	21.6	−10.4	8.34	0.39	6.66	0.31	347	16.1	5.2
1/17/24	H. L.	8	♀	19.3	−10.6	8.73‡	0.45	6.18	0.32	286	14.8	4.6
12/13/23	H. G.	11	♂	27.5	−10.7	9.75	0.35	7.81	0.28	228	8.3	2.9
11/17/22	I. Bo.	9	♂	20.7	−10.7	9.76‡	0.47	5.29	0.26	...	....	...
11/ 6/24	L. C.	6	♀	18.0	−11.3	9.30	0.52	7.08	0.39	318	17.7	4.5
4/10/24	M. M.	7	♂	17.9	−11.8	8.71	0.49	7.79	0.44	280	15.6	3.6
3/ 7/24	B. B.	5	♀	12.0	−11.8	7.17‡	0.60	5.24	0.44	...	....	...
8/21/24	S. K.	10	♂	26.8	−12.1	16.17‡	0.60	14.28	0.53	356	13.3	2.5
4/10/24	J. M.	13	♂	27.5	−12.1	10.95	0.40	9.52	0.35	398	14.5	4.2
7/31/24	N. G.	7	♂	15.0	−12.3	10.33‡	0.69	8.02	0.53	258	17.2	3.2
2/ 1/23	R. D.	10	♀	19.1	−12.3	9.08‡	0.42	5.87	0.31	...	....	...
9/27/23	B. G.	8	♀	19.1	−13.6	9.99	0.52	5.27	0.28	272	14.2	5.2
12/28/23	R. B.	6	♂	16.4	−14.1	8.06	0.49	6.04	0.37	...	....	...
Average.....							0.49		0.37		14.6	4.0
More than 15 per cent Below Average												
10/17/24	L. C.	6	♀	17.1	−15.8	8.35	0.49	7.17	0.42	265	15.5	3.7
5/15/24	D. Y.	7	♀	17.3	−16.0	8.31	0.48	7.26	0.42	281	16.2	3.9
7/31/24	S. K.	10	♂	25.4	−16.7	15.33‡	0.60	11.80	0.46	393	15.5	3.3
11/11/22	I. Be.	11	♀	26.0	−17.2	7.67‡	0.30	5.49	0.21	...	....	...
2/ 7/24	L. P.	8	♀	22.6	−19.8	8.74	0.39	6.04	0.27	241	10.7	4.0
11/22/23	R. N.	11	♀	25.2	−25.0	7.98	0.32	6.65	0.26	271	10.8	4.1
12/14/23	A. Go.	8	♀	17.9	−25.7	6.53	0.36	6.19	0.35	220	12.3	3.6
Average.....							0.42		0.34		13.5	3.8

* In this column, ♀ indicates female; ♂, male
† Vigorous normals.
‡ Rose's figures.

A COMPARISON OF THE PIRQUET, MANTOUX, RING AND TUBERCUMET TESTS IN LYMANHURST CHILDREN *

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In spite of the progress that has already been made, the diagnosis of tuberculosis in its minimal stage, when its recognition and treatment offers the greatest benefit to the patient, is still extremely difficult. In the vast majority of children, the presence or absence of tuberculous infection usually may be determined by the application especially of the Pirquet or Mantoux tests. These tests, although undoubtedly specific, when positive show only that at some time the person has been infected by the bacillus of tuberculosis, but give no information as to the activity of the tuberculous lesion. In addition, a negative result from the beforementioned tests does not exclude tuberculosis, particularly in advanced or terminal stages of the disease and also in children for a variable period following certain diseases such as measles, scarlet fever, diphtheria, influenza, erysipelas or typhoid fever. The Pirquet and Mantoux tests, nevertheless, continue to be of clinical value, in spite of their failure to give any information as to whether or not a known tuberculous infection is active or inactive.

TUBERCUMET TEST

Recently, an additional test for tuberculosis has been developed in the department of bacteriology at the University of Minnesota by Larson, Montank and Nelson [1] which, as a result of clinical studies by Myers,[2] has been found to be positive in a high percentage of cases having definite active tuberculosis. In addition, the so-called tubercumet test also deserves clinical study to establish fully its value in differentiating active from inactive types of tuberculosis.

A study of these four tests was undertaken at the Lymanhurst School for tuberculous children in Minneapolis, on a considerable group of children who were studied exhaustively from the standpoint of tuberculosis.

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1. Larson, M. P.; Montank, I. A., and Nelson, E.: The Precipitin Test in the Diagnosis of Tuberculosis, Proc. Soc. Exper. Biol. & Med. **20**:350, 1923.

2. Myers, J. A.: A Study of the Clinical Findings and Ring Test in 500 Cases Examined for Tuberculosis, Am. Rev. Tuberc. **11**:71, 1925.

The examination of these children included careful histories, repeated physical examinations, stereoscopic chest plates, daily temperature records and tuberculin tests. The data are complete for 218 children, the results of which are reported in this paper (tables 1 to 4 inclusive). Of these children, sixty-five (table 1) had negative Pirquet reactions. The Mantoux tests in this group also proved negative in 86.8 per cent of the cases, and positive in 13.2 per cent. This observation is in agreement with the usual experience that a certain small percentage of children may have a positive Mantoux test in spite of the fact that the Pirquet is negative. The ring and tubercumet tests, as may be seen from table 1, were negative in 100 per cent of the children included in this group. As the result of careful and exhaustive examinations we were

TABLE 1.—*Observations on Children Having Negative Pirquet Tests*

	Mantoux		Ring Test		Tubercumet		
No. of Cases	% Positive	% Negative	% Negative	% Positive	% Negative	% Positive	Remarks
65	13.2 (7)*	86.8 (46)	100.0 (65)	0.0 (0)	100.0 (58)	0.0 (0)	No evidence of active tuberculosis in this group. Tuberculous infection in 7

* Number of cases tested.

TABLE 2.—*Observations on Children Having Positive Pirquet Tests*

	Mantoux		Ring Test		Tubercumet		
No. of Cases	% Positive	% Negative	% Negative	% Positive	% Negative	% Positive	Remarks
116	96.4 (105)*	3.6 (4)	100.0 (116)	0.0 (0)	100.0 (41)	0.0 (0)	No evidence of active tuberculosis in this group. Tuberculosis infection in 116. Healed tuberculosis in 4

* Number of cases tested.

unable to find any evidence of active tuberculosis in any of these sixty-five children. Without exception, the ring and tubercumet tests, which are known to be positive in patients having active tuberculosis, were negative in 100 per cent of these cases. Negative ring and tubercumet reactions, therefore, are to be expected in healthy persons in whom there is absolutely no evidence of active tuberculosis.

Among the children admitted to Lymanhurst, 116 (table 2) were diagnosed as having juvenile or hilum tuberculosis. The diagnosis in these cases was based on positive Pirquet and Mantoux reactions, roentgen-ray evidence of enlargement and calcification of bronchial lymph nodes, undernutrition, frequent colds, definite exposure to open cases of tuberculosis and occasional elevations in temperature. These children were not considered to have active tuberculosis clinically, but merely a

quiescent probably nonprogressive tuberculous infection of the bronchial lymph nodes. The Mantoux reaction (table 2) was in agreement with the Pirquet in 96.4 per cent of the cases, and disagreed in 3.6 per cent. The agreement between the two tests was higher among the children having a positive than among those having a negative Pirquet. It is evident from the result of these two tests that tuberculous infection had occurred at some previous date in all of the 116 children in this group. From careful and repeated examination, however, we were unable to find any evidence of active tuberculosis in any of these children. In four cases, though, tuberculosis of bone and glands had existed, but was considered entirely healed from a clinical standpoint at the time the various tests were applied. The ring and tubercumet tests (table 2) proved negative without exception in this entire group of children. It

TABLE 3.—*Observations on Children Having Positive Ring Tests and Definite or Suspected Active Tuberculosis*

	Pirquet		Mantoux		Tubercumet		
No. of Cases	% Positive	% Negative	% Positive	% Negative	% Positive	% Negative	Remarks
37	62.1 (23)	37.9 (14)	70.6 (26)	29.4 (11)	64.7 (24)	35.3 (13)	Later ring and tubercumet tests negative in 26 of these children; there is no evidence of active tuberculosis in these 26; initial positive ring and tubercumet tests explained as due to rhinitis, bronchitis, tonsillitis, sinusitis and myositis; 10 of 11 remaining cases are known to have tuberculosis (see table 4)

is evident, therefore, that the mechanism responsible for a positive Pirquet and Mantoux test does not influence the ring and tubercumet tests in children having no clinical evidence of active tuberculosis. It appears, therefore, that in cases of completely healed and quiescent tuberculosis or inactive tuberculous infection, the ring and tubercumet tests may be expected to be negative.

SIGNIFICANCE OF TESTS

The question arises, therefore, as to the significance of positive ring and tubercumet tests. Positive reactions occurred in thirty-seven cases (table 3), of which the Pirquet and Mantoux were positive in 62.1 and 70.6 per cent of cases respectively. On repeating the ring and tubercumet tests on this group, a later persistent negative result was obtained in twenty-six of these thirty-seven children. Careful examination of this group revealed no evidence of active tuberculosis in any of these twenty-six children. The temporary positive ring and tubercumet reac-

tions in these children apparently were due to acute rhinitis, tonsillitis, bronchitis, sinusitis and myositis, existing at the time the first tests were taken. With the subsidence of these acute infections the ring and tubercumet reactions became negative, and remained negative during the continuance of good health of these twenty-six children. This observation shows that acute infection may disturb the ring and tubercumet tests, but the disturbances due to these diseases are only temporary in character. In this study the observation was made that the ring test apparently is more sensitive and more easily disturbed by acute respiratory infections than the tubercumet test. Thus, among the thirty-seven children having initial positive ring test, the initial tubercumet test was positive in twenty-four and negative in thirteen.

TABLE 4.—*Ten Children Having Definite Tuberculosis Active and Inactive and One Undiagnosed*

No. of Cases	Ring Tests		Tubercumet		Pirquet	Mantoux	Diagnosis
	First	Final	First	Final			
1	Pos.	.....	Pos.	.....	Pos.	Pos.	Active tuberculosis of humerus
2	Pos.	.....	Pos.	.....	Neg.	Pos.	Tuberculous meningitis
3	Pos.	.....	Pos.	.....	Neg.	Pos.	Tuberculous peritonitis
4	Pos.	.....	Pos.	.....	Pos.	Pos.	Active tuberculosis of metatarsal
5	Pos.	.....	Neg.	.....	Pos.	Pos.	Healed Potts (cold)
6	Pos.	Neg.	Neg.	Neg.	Pos.	Pos.	Healed tuberculosis of dorsal spine; cold at time of first ring test
7	Pos.	.....	Neg.	.....	Pos.	Pos.	Probably healed tuberculosis of knee
8	Pos.	Neg.	Pos.	Neg.	Pos.	Pos.	Healed tuberculous glands; cold at time of first ring test
9	Pos.	Neg.	Neg.	Neg.	Pos.	Pos.	Healed tuberculous glands; cold at time of first ring test
10	Pos.	Neg.	Neg.	Neg.	Pos.	Pos.	Healed tuberculous gland; cold at time of first ring test
11	Pos.	Pos.	.....	Neg.	Neg.	.....	Chronic parotitis; etiology?
12	Neg.	.....	Neg.	.....	Pos.	Pos.	Healed tuberculosis of cervical glands
13	Neg.	.....	Neg.	.....	Pos.	Pos.	Healed tuberculosis of hip
14	Neg.	Neg.	Neg.	Neg.	Pos.	Pos.	Healed tuberculosis of cervical glands
15	Neg.	.....	Neg.	.....	Neg.	Pos.	Tuberculosis of skin

In the remaining eleven of these thirty-seven children having positive ring and tubercumet reactions, a more detailed consideration is necessary. The observations are tabulated in table 4. In four cases having known active tuberculosis (table 4) of the humerus, meninges, peritoneum and metatarsal bones respectively, the ring and tubercumet tests were uniformly positive. At the time these tests were taken, there was no evidence of an acute nontuberculous infection in any of these four children. These results were interpreted as indicating the presence of active tuberculosis in each of these four children, which was fully confirmed clinically. To date, it has been impossible to repeat the ring and tubercumet tests in these children, due to the fact that three have been sent to a sanatorium and one has died.

In cases 5 to 10, inclusive (table 4), all of the patients had tuberculosis of bone or glands considered clinically as healed, the first ring tests were positive. The tubercumet test was positive in only one of

these children (case 8) however. In five of these six children the initial positive ring test apparently was due to acute colds existing at the time the tests were taken. This view is supported by the fact that later ring tests (and also the tubercumet tests) were negative in four of these children after the acute respiratory infection had subsided. For one child (case 7) the positive ring test is unexplained, and to date a repetition of the test has not been made. Another patient (case 11), has a chronic parotitis of undetermined etiology, and in this instance there is no satisfactory explanation of the persistently positive ring test. Since in this case, however, the tubercumet and Pirquet tests are negative, the possibility of the parotitis being due to tuberculosis is doubted.

The last four cases in table 4 were entirely free from acute infections at the time the ring and tubercumet tests were taken, and in each of these children the existing tuberculous condition was considered as definitely healed. For these four children the ring and tubercumet tests were uniformly negative, as expected.

To summarize the findings in the fourteen children, the ring and tubercumet tests were positive in four known to have definite active tuberculosis of various types. In four having definitely healed tuberculosis of bone and glands, these tests were also negative. For the remaining seven children, a temporary positive ring test occurred in five, apparently as the result of acute respiratory infections. In two instances (cases 7 and 11), no satisfactory explanation for the positive ring test is apparent.

COMMENT

As a result of this study, it appears that the ring and tubercumet tests may prove of some definite value in differentiating to some extent between active and inactive types of tuberculosis. Particularly in children having positive Pirquet and Mantoux reactions combined with such findings as to justify a diagnosis of juvenile tuberculosis, negative ring and tubercumet tests probably indicate that the tuberculous focus is clinically inactive. In children having tuberculosis of bone and glands, a negative ring and tubercumet test probably indicates that the process is healed. Positive ring and tubercumet tests apparently are of significance only when these tests remain persistently positive in children who have positive Pirquet or Mantoux reactions, and who have no evidence of acute, nontuberculous infections.

CONCLUSIONS

1. In healthy children having negative tuberculin tests, the ring and tubercumet tests are uniformly negative.

2. In children not suffering from acute infections, but having positive Pirquet and Mantoux tests, together with such clinical findings as

enlargement and calcification of the bronchial lymph nodes, slight occasional elevation in temperature, undernutrition and a history of exposure to tuberculosis but with no evidence of clinically active tuberculosis, the ring and tubercumet tests are negative. Under such circumstances, negative ring and tubercumet tests apparently are confirmatory evidence that the tuberculous focus is inactive and thus of definite clinical value.

3. In definitely active tuberculosis the ring and tubercumet tests usually are positive.

4. Positive ring and tubercumet tests are not specific tests for active tuberculosis, for they may become temporarily positive as the result of acute nontuberculous infections.

5. To be of significance the positive ring and tubercumet tests should be persistently positive. Under such circumstances when certain chronic nontuberculous infections such as pyelocystitis, osteomyelitis and others are excluded, persistently positive ring and tubercumet tests should cause one to suspect strongly the presence of active tuberculosis.

6. A diagnosis of active tuberculosis on the basis of positive ring and tubercumet tests alone should not be made.

7. In making a diagnosis of active tuberculosis, the results of the ring and tubercumet tests should be used with and not to the exclusion of other established methods of examination.

8. Tests such as the ring and tubercumet reactions, which are known to be positive in cases of active tuberculosis and neg[illegible] in healed tuberculosis, undoubtedly will prove of value when their limitations are fully understood.

DIGITALIS THERAPY IN CARDIAC DECOMPENSATION IN CHILDREN *

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AND
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Digitalis is often believed to be ineffectual in the treatment of cardiac disease in children. The most probable explanation for this belief is that the doses commonly used have been too small, for McCulloch and Rupe [1] have demonstrated that both normal children and those suffering from heart disease require from 10 to 100 per cent more digitalis per pound of body weight than do adults before electrocardiographic or other signs of digitalization are produced. Our studies of twenty-six children suffering from severe myocardial failure confirm this report, and lead us to the conclusion that even larger doses are beneficial in causing a loss of edema and an increase in the patient's comfort. Digitalis will not, of course, repair the myocardial damage, but a comparison between the fate of children treated with the drug and that of those who did not receive it would seem to indicate that the administration of digitalis will to some extent prolong life by providing an opportunity for compensation.

MATERIAL

These twenty-six patients (table 1) suffered from rheumatic endocarditis and myocarditis, and represent all the cases of severe cardiac decompensation admitted to this hospital from 1921 to 1926. All were orthopneic and edematous, and half of them (thirteen) had marked ascites. None of the cases of rheumatic endocarditis in which the symptoms of decompensation were absent or slight were included. These children were from 3 to 13 years of age, and had had their first attack of acute rheumatic fever or chorea from three months to five years previously. Of these twenty-six patients, twenty-one had had rheumatic fever, in some instances chorea also, and the remaining five had had chorea alone. Symptoms and signs of heart disease had been present from three to thirty months before decompensation developed.

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* From the department of pediatrics of the Johns Hopkins University School of Medicine, and the Harriet Lane Home of the Johns Hopkins Hospital, Baltimore. Read before the American Pediatric Society, Niagara Falls, Canada, May 31, 1926.

1. McCulloch, H., and Rupe, W. A.: Studies on the Dosage of Digitalis in Children, Am. J. M. Sc. **162**:231-237, 1921; idem, On the Tolerance of Children for Digitalis, South. M. J. **15**:381-385, 1922.

In seventeen patients, severe myocardial failure occurred in less than six months after the first attack of rheumatic fever. Of the fourteen deaths in this series, six occurred within six months of the initial rheumatic manifestation. Necropsies were performed on nine of the fourteen children who died, and in each instance Aschoff bodies, the typical lesions of rheumatic infection, were found in the myocardium.

CLINICAL EFFECT OF DIGITALIS IN CHILDREN

Sixteen of these patients were given various amounts of digitalis. Our criterion of the desired effect of digitalis therapy was a loss of edema, and we considered nausea or a definite slowing of the rate of the

TABLE 1.—*Material*

Therapy	Patient	Age at Onset of Decompensation (in Years)	Weight (Without Edema) (in Pounds)	Age at First Attack of Rheumatic Fever or Chorea (in Years)	Number of Attacks of Rheumatic Fever (R) or Chorea (C)	Duration of Heart Disease Before Decompensation Developed (in Months)	Duration of Life After First Attack of Rheumatic Fever or Chorea (in Months)
Rest in bed and digitalis	A. F.	12	54	11	1 R	12	Still alive (50)
	L. D.	10½	60	10	2 R	9	Still alive (18)
	J. B.	5½	37	5	1 R	4	Still alive (24)
	H. L.	9½	52	9	2 R	4	Still alive (12)
	G. S.	7	37	6½	2 R	3	Still alive (25)
	R. S.	12½	86	8	3 R, 1 C	18	?
	B. R.	6½	46	6	1 R	5	Still alive (40)
	J. S.	11	62	10	2 R	12	Died (16)
	M. R.	11½	54	9½	1 R, 1 C	24	Died (36)
	V. L.	13	86	8	3 R	8	Died (60)
	E. D.	11	60	6½	4 C	12	Died (60)
	I. G.	6½	44	6	1 C	5	Died (12)
	M. C.	6	36	5½	1 R	4	Died (11½)
	J. J.	9	48	8½	1 R	6	Died (6)
	C. B.	11	?	10½	1 R	3	Died (3½)
	J. H.	11½	60	?	?	11	Died (?)
Rest in bed alone	G. T.	8½	37	5	1 R	30	Still alive (90)
	K. W.	11	74	10½	2 R	8	Still alive (26)
	M. S.	11	44	10	2 R	6	Died (12)
	L. F.	8½	50	8	1 C	3	Died (3)
	M. B.	5½	?	5	1 R	3	Died (3)
	S. S.	8	46	7½	1 R	5	Died (8)
	M. G.	3	33	2½	2 R	4	Died (6)
	D. D.	3½	30	3	1 R	3	Died (3)
	R. F.	7	43	6½	1 R	5	Died (?)
	K. R.	9½	54	9	1 R	9	Died (20)

heart as indications for stopping the administration of the drug. The occurrence of nausea seemed to be a reliable sign that the patient had received sufficient digitalis to produce the desired effect; it is one of the earliest symptoms of intoxication, almost invariably developing before the pulse rate is markedly reduced, and appears to have no deleterious effect on the patient. Changes in the electrocardiogram are, of course, a definite indication of the absorption of digitalis but are not as constant an index of its therapeutic effect as are clinical symptoms. The amount of digitalis per pound of body weight required to cause an alteration in the T wave varies in different persons, and this quantity is often insufficient to produce the desired clinical effect. Therefore, it is really

more accurate as well as much simpler to use nausea as a criterion than to obtain electrocardiographic records at frequent intervals.

The quantity of digitalis which Eggleston [2] found to be required in twenty-four hours to produce the desired effect in adults was 0.15 cat units per pound, or in terms of the dried leaves of digitalis,[3] 0.24 grains per pound. We gave, during the first twenty-four hours, an amount of digitalis per pound of body weight approximately 50 per cent greater than is generally given to adults, usually in doses of 3 grains (0.2 Gm.) of the dried leaves in capsules by mouth every four hours. Chart 1 illustrates three points which we wish to emphasize: First, the increase

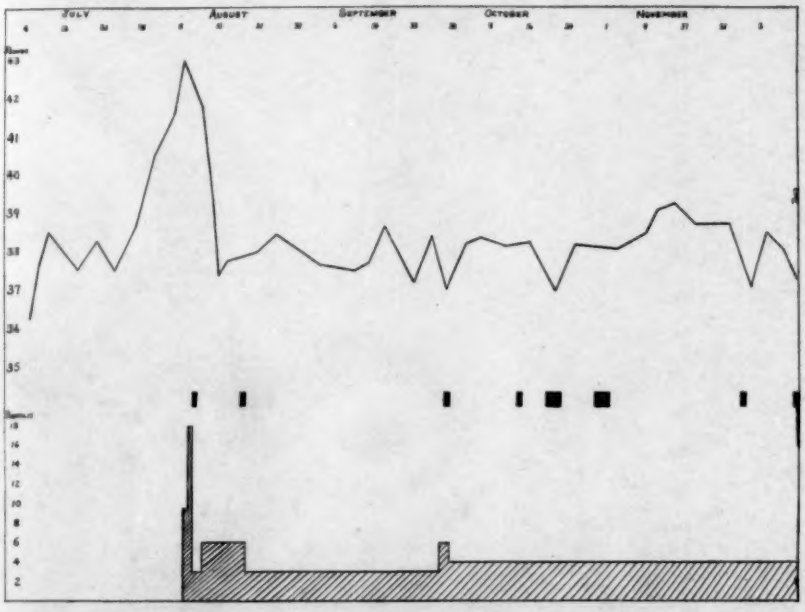

Chart 1.—Weight curve of M. C., a girl, aged 6 years. Solid blocks indicate vomiting; hatched areas indicate amounts (grains) of digitalis administered.

in edema during the four weeks during which the child (case 1) remained in bed and did not receive digitalis; second, the complete loss of edema in one week following the administration of the drug, and third, the amount required to maintain the effect of digitalis.

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2. Eggleston, C.: Digitalis Dosage, Arch. Int Med. **16**:1-32 (July) 1925; idem, Administration of Digitalis by "Eggleston Method," J. A. M. A. **74**:733-734 (March 13) 1920. Robinson, G. C.: The Therapeutic Use of Digitalis, Medicine, **1**:1-137, 1922.

3. The preparation of the dried leaves of digitalis (L. V. Hopkins, Williams street, New York City) employed in this study has been used in this hospital for several years, and found to be of uniform strength.

REPORT OF CASES

CASE 1.—M. C., a girl, aged 6 years, weighed 36 pounds (16.3 Kg.) and had had rheumatic heart disease for four months before decompensation developed. She was then admitted to this hospital. Rest in bed for four weeks did not improve her condition; in fact, her edema increased to the extent of 7 pounds (3.2 Kg.). Digitalis therapy was then commenced. During the first two days, 27 grains of the dried leaves were given; then, because the child vomited, the dose was reduced to 3 grains per day for the next two days and increased to 6 grains daily thereafter. The patient vomited after 6 grains per day had been given for nine days, but she remained free from nausea for thirty-nine days after the dose had been reduced to 3 grains daily. The patient's weight fluctuated about 1½ pounds during this period, so the digitalis was increased to 6 grains per day for two days and then reduced to 4 grains daily. This amount was probably slightly

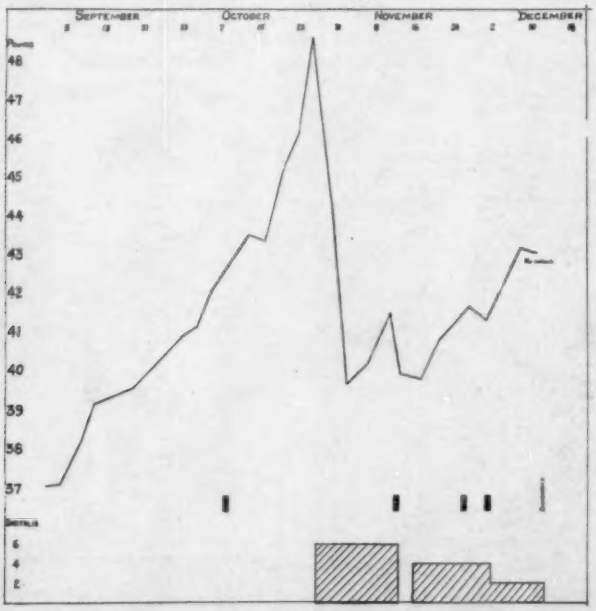

Chart 2.—Weight curve of G. S., a girl, aged 7 years. Solid blocks indicate vomiting; hatched areas indicate amounts (grains) of digitalis administered.

more than sufficient to maintain the effect of the drug for, although the patient's pulse was never less than 70 per minute, she vomited occasionally during the eleven weeks in which she received this dosage. The edema never reaccumulated, but her general condition did not improve and she died after eight months in the hospital. At necropsy the heart was hypertrophied and dilated; the pericardium was adherent, and extensive pleural adhesions bound the pericardium and lungs to the chest wall. The mitral valve, the chordae tendinae and the left auricular wall were thickened and scarred. Small vegetations were present on the tricuspid valve, and Aschoff bodies were found in the myocardium. In addition, the middle and lower lobes of the right lung were consolidated.

Chart 2 (case 2) illustrates the rate at which edema may accumulate when digitalis is not given, even though the child remains in bed, and

also the rapidity with which it may be lost during the administration of digitalis.

CASE 2.—G. S., a girl, aged 7 years, weighed 42 pounds (19.1 Kg.), and had had rheumatic heart disease for three months before she became edematous and was admitted to this hospital. During rest in bed for seven weeks, her weight increased 11 pounds (5 Kg.) and her general condition became worse. Three days after the patient had taken 6 grains per day the weight had decreased 4 pounds (1.8 Kg.), and after seven days of this daily dosage a total of 9 pounds (4.1 Kg.) had been lost. Nausea did not develop until the seventeenth day. Digitalis was then discontinued for three days and thereafter administered in daily doses of 4 grains. Occasional vomiting persisted but disappeared after this

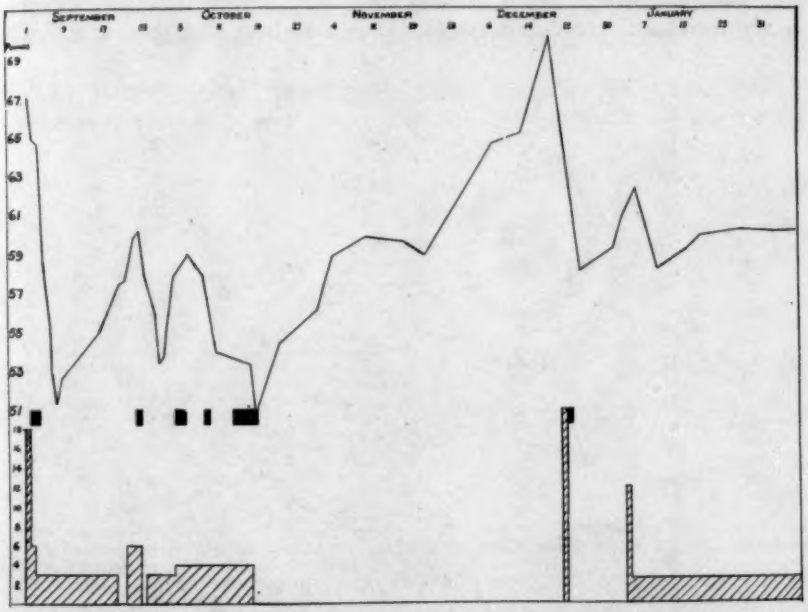

Chart 3.—Weight curve of E. D., a girl, aged 11 years. Solid blocks indicate vomiting; hatched areas indicate amounts (grains) of digitalis administered.

amount had been decreased to 2 grains per day. During the last five weeks of this patient's stay in the hospital, she gained 3 pounds (1.4 Kg.) in weight, but this increase was not due to edema. Her heart has remained compensated during the last year and a half.

The effect of digitalis is also well illustrated in chart 3 (case 3).

CASE 3.—E. D., a girl, aged 11 years, rapidly lost 15 pounds (6.8 Kg.) of edema following the administration of 18 grains during the first twenty-four hours, 6 grains on the second day and 3 grains daily thereafter. Contrary to our experience with other children, a daily dose of 3 grains was insufficient to prevent the reaccumulation of edema, for in the following three weeks she gained 8 pounds (3.6 Kg.). However, after 6 grains per day had been given for three days the edema disappeared again, only to return when the daily dose was reduced to 3 grains. Four grains per day caused a loss of edema, but, as vomiting

developed and persisted on this dosage, digitalis was discontinued. During the next two months, when no digitalis was given, the edema steadily increased to the extent of 19 pounds (8.6 Kg.). Twenty grains of digitalis and 8 grains of theophylline were then administered in twenty-four hours, and within three days all of the edema had disappeared. The impression given by the chart that the loss of weight preceded the administration of digitalis is probably erroneous, for the child was only weighed at weekly intervals. The part played by the theophylline in causing the loss of edema is difficult to evaluate. This drug was used in only two of our cases, and in one it appeared to increase the effect of digitalis. The edema began to reaccumulate as soon as the digitalis was discontinued, but disappeared when the administration of the drug was resumed. The child was then given 3 grains per day for fifty days and there was no further increase of edema.

When digitalis is given in sufficiently large doses, the loss of edema is accomplished within one week. It is also true that edema will dis-

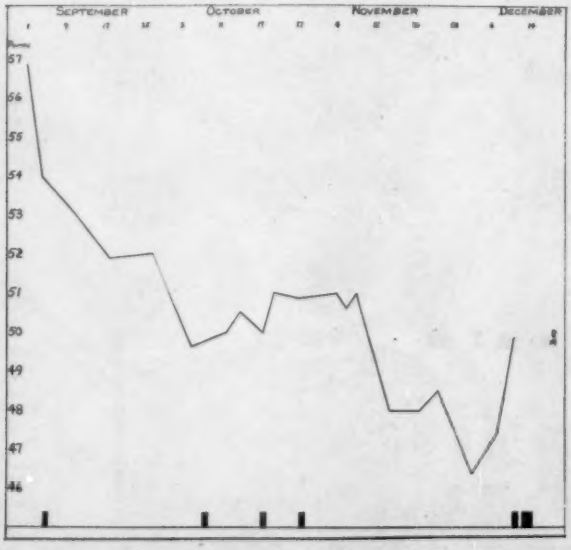

Chart 4.—Weight curve of S. S., a girl, aged 8 years. Solid blocks indicate vomiting.

appear as a result of rest in bed without digitalis but, as may be seen in chart 4 (case 4), a long period is often necessary.

CASE 4.—S. S., a girl, aged 8 years, was admitted to the hospital in 1921 before the present method of digitalis therapy was begun. Although her cardiac disease, so far as could be determined clinically and pathologically, was not as extensive as that of the patient whose course is illustrated in chart 1, two and one-half months of rest were required before she lost 11 pounds (5 Kg.) of edema. This loss was neither complete, for ascites persisted, nor permanent, for in the next three weeks 4 pounds (1.8 Kg.) of fluid—edema and ascites—reaccumulated. She died after four months in the hospital. At necropsy, the heart was hypertrophied and dilated and vegetations were present on the mitral and tricuspid valves. Aschoff bodies and hemorrhages were found in the myocardium. There were fibrinous pleural and peritoneal adhesions, and lobular pneumonia.

The physical comfort of all of these patients was markedly increased by digitalis therapy, a feature which cannot be illustrated in tables and charts, but which, nevertheless, we think is one of the most striking benefits to be derived from this drug.

DETERMINATION OF THE AMOUNT OF DIGITALIS REQUIRED FOR A DEFINITE EFFECT

The body weight, exclusive of edema, of the patients in this series (table 2) varied from 33 to 86 pounds (from 15 to 39 Kg.), and the usual initial dosage was 3 grains (0.2 Gm.) of the dried leaves in capsules by mouth every four hours for six doses, or from 0.3 to 0.5 grains per pound of body weight during the first twenty-four hours. In every

TABLE 2.—*Amounts of Dried Digitalis Leaves Necessary for Clinical Effect*

Patient	Weight	Maximal Dose Within 24 Hours (in Grains)	Amount Required for Digitalization *	
			Total Amount (in Grains)	Amount per Pound of Body Weight (in Grains)
A. F.	54	18	18	0.333
M. R.	54	18	36	0.666
R. S.	86	18	†	.....
J. S.	62	18	30	0.483
L. D.	60	18	†	.....
J. J.	48	18	24	0.500
I. G.	44	18	18	0.409
M. C.	36	18	28	0.770
V. L.	86	18	‡	.....
E. D.	51	18	18	0.353
H. L.	52	24	24	0.461
B. R.	46	14	49	1.000
J. B.	37	12	18	0.486
C. B.	..	12	30	.....
J. H.	60	12	‡	.....
G. S.	37	8	†	.....

* If more than twenty-four hours were required for effect, three grains for each day have been subtracted to allow for excretion of the drug.

† Accurate determination was impossible, as small amounts were given over a long period of time.

‡ No effect demonstrated.

instance a loss of edema was produced, and in 70 per cent nausea did not develop. In the latter patients, the administration of digitalis was continued in doses of from 4 to 18 grains per day until nausea appeared. To determine the amount of digitalis which produced a definite effect, the quantity which the patient probably excreted was subtracted from the total dosage of the drug administered before nausea developed. As will be shown later, the daily excretion of digitalis in children is probably about 3 grains, as this amount may be given daily for long periods of time to children who have been digitalized without producing nausea or other signs which would indicate an increased accumulation of the drug in the body. The net amount of digitalis which produced a definite clinical effect without signs of intoxication (total quantity minus excretion) in this series has varied from 18 to 49 grains or, when divided

by the body weight, from 0.3 to 1.0 grains per pound. The average net amount required to produce complete digitalization was 0.5 grains per pound of body weight, or twice the quantity which is usually sufficient in adults.

Because of this great difference in the amounts of digitalis which are necessary to produce the desired effect in children, we believe that the practice commonly used in adults of calculating the dosage of this drug on the basis of the patient's body weight is not applicable to children. The individual tolerance of each patient for digitalis should be determined, for the "human unit," at least in children, is not as constant as the "cat unit." It is possible that this variation in the amount of the

TABLE 3.—*Excretion* *

Patient	Weight Without Edema (in Pounds)	Maximal Daily Dose Tolerated Without Symptoms of Intoxication After Initial Effect (in Grains)	Length of Time Administered (in Days)	Daily Dose (in Grains) Which Induced Symptoms of Intoxication	Symptoms of Intoxication
E. D.	60	3	50	4	Repeated vomiting after one day
I. G.	44	3	8	4	Vomiting and pulse rate below 60 after receiving 36 grains in nine days
M. C.	38	3	40	4	Repeated vomiting
J. S.	62	3	20	..	
M. R.	54	3	111	6	Auricular fibrillation
J. H.	60	4	40	..	
G. S.	42	..	..	4	Repeated vomiting; pulse rate 60 per minute
J. B.	37	..	..	4	Pulse rate 60 per minute; extra systoles
R. S.	86	..	..	4	Vomiting and extra systoles
H. L.	52	..	..	4	Repeated vomiting; pulse rate 60 per minute after one day
B. R.	46	..	..	4½	Vomiting after four days
L. D.	60	..	..	6	Pulse rate below 60 per minute after twenty-one days

* In the remaining cases the digitalis was discontinued after the initial large dose; consequently, no estimation of the daily tolerance could be made.

drug required for the digitalization of decompensated children, which is in such marked contrast to the uniformity of the quantity necessary to maintain the effect of digitalis, depends on an increased rate of excretion during the period in which the patient is losing edema and is passing a large volume of urine. Perhaps the simplest method of administration of digitalis in children is to give, regardless of the patient's age and body weight, 3 grains (0.2 Gm.) of the dried leaves in capsules by mouth every six hours until nausea develops (usually after four to eight doses). The exact number of doses required by an individual patient cannot be forecast on the basis of age and weight, but this method of administration based on the patient's tolerance is safe and efficacious. As soon as nausea or marked slowing of the pulse occurs, the dose of digitalis should be reduced to 1½ grains (0.1 Gm.)

twice a day. The latter quantity may usually be continued indefinitely. However, should nausea or marked slowing of the pulse develop while this reduced dosage is being given, digitalis should be discontinued and not readministered until one to two days after all symptoms of intoxication have disappeared. Preliminary rest in bed before digitalis therapy is begun does not appear to be of any advantage.

For patients who have been vomiting before digitalis therapy is begun, and who consequently cannot retain the drug if administered by mouth, 30 minims (2 cc.) of the tincture of digitalis diluted with 1 ounce (30 cc.) of physiologic sodium chloride solution may be given by rectum every six hours until the pulse rate is definitely reduced (usually after four to eight doses). The amount should then be decreased to 15 minims (1 cc.) of the tincture, diluted with 1 ounce (30 cc.) of physiologic sodium chloride solution twice a day to replace the daily excretion. As vomiting obviously cannot be used as an index of the

TABLE 4.—*Comparison of Results*

Treatment	Number of Patients	Number of Deaths	Average Duration of Life After First Attack of Rheumatic Fever or Chorea, in All Cases * (in Months)	Average Interval Between First Attack of Rheumatic Fever or Chorea and Death, in Fatal Cases (in Months)
Digitalis and rest in bed.....	16	9 (56%)	18 (3½—60)†	14 (3½—60)
Rest in bed alone.....	10	8 (80%)	8 (3—90)	6 (3—20)

* As several of these patients are still alive (table 5), these figures represent the duration of life only up to the time of writing.

† Minimal and maximal number of months are given in parentheses.

effect of digitalis in these patients, the pulse rate must be measured at intervals of four hours. This rectal dosage is equivalent to that outlined in the foregoing for oral administration, and the results obtained in patients to whom digitalis has been given by rectum indicate that the drug is equally well absorbed and tolerated.

AMOUNT OF DIGITALIS EXCRETED DAILY AFTER DIGITALIZATION

As may be seen in table 3 and charts 1 and 3, all of the patients studied were able, after digitalization, to take 3 grains of dried digitalis leaves daily (1½ grains twice daily) for one to sixteen weeks without developing symptoms of intoxication. In all but one of the patients who had been digitalized, 4 grains of digitalis daily produced vomiting or marked slowing of the pulse within a few days. This exceptional child could apparently tolerate much larger amounts of the drug, for she received 6 grains per day for three weeks before symptoms of intoxication appeared. Three grains would, therefore, seem to be the safe maximal daily dose after digitalization; this amount probably represents

the quantity of digitalis which is excreted daily. As long as these patients received 3 grains per day, the effect of the initial digitalization usually remained, as was evidenced by the fact that the edema which had been lost did not reaccumulate, even in those children whose cardiac damage was so extensive that they died within the following two months.

COMPARISON OF RESULTS

The impression given by table 4 that digitalis therapy decreased the case fatality in cardiac decompensation is very probably fallacious, for the courses of the patients who received the drug have not been observed

TABLE 5.—*Comparison of Results*

Patients Receiving Digitalis	
A. F.	Well 3 years after discharge from the hospital
L. D.	Well 1 year after discharge
J. B.	Well 1½ years after discharge
H. L.	Well 6 months after discharge
G. S.	Well 1½ years after discharge
R. S.	Discharged improved after 10 weeks in the hospital; present state unknown
B. R.	Well 3 years after discharge
J. S.	Discharged improved; died at home 4 months later
M. R.	Died after 12 months in the hospital
V. L.	Died after 9 months in the hospital
E. D.	Died after 9 months in the hospital
I. G.	Died after 9 months in the hospital
M. C.	Died after 1 month in the hospital
J. J.	Died after 6 days in the hospital
C. B.	Died after 3½ months in the hospital
J. H.	Died after 3 months in the hospital
Patients Receiving No Digitalis	
G. T.	Discharged slightly improved with ascites still present after 6 weeks in the hospital; still alive 5 years after discharge
K. W.	Well 1½ years after discharge
M. S.	Died after one month in the hospital
L. F.	Died after 18 days in the hospital
M. B.	Died after 2 days in the hospital
S. S.	Died after 3½ months in the hospital
M. G.	Died after 2 months in the hospital
D. D.	Died after 3 weeks in the hospital
R. F.	Discharged after 6 weeks in the hospital; died later, date unknown
K. R.	Discharged improved after 6 weeks; died one year later

as long as those of the children not treated with digitalis. It is evident, however, that the patients treated with digitalis have lived at least ten months longer than those in the other group, while in the treated patients who died, the fatal result was apparently postponed an average of eight months longer than in the untreated group. The course of all of the twenty-six patients is summarized in table 5.

CONCLUSIONS

1. The administration of comparatively large doses of digitalis to edematous children suffering from rheumatic heart disease usually causes a loss of edema, an increase in the patient's comfort and a prolongation of life.

2. An accumulation of 0.5 grains of dried digitalis leaves per pound of body weight will usually produce the desired effect in children. A subsequent daily dosage of 3 grains, which probably represents the daily excretion, will usually maintain this effect without causing symptoms of intoxication (nausea or marked slowing of the pulse).

3. For children suffering from cardiac decompensation, 3 grains (0.2 Gm.) of the dried leaves of digitalis may be given by mouth in capsules every six hours until nausea develops (usually after four to eight doses). The amount should then be decreased to 1½ grains (0.1 Gm.) of the dried leaves twice a day, to replace the amount which the patient excretes daily. This dosage may usually be continued indefinitely. However, should nausea or marked slowing of the pulse develop on this reduced dosage, digitalis should be discontinued and not readministered until one to two days after all symptoms of intoxication have disappeared. For patients who have been vomiting before digitalis therapy is begun, 30 minims (2 cc.) of the tincture of digitalis diluted with 1 ounce (30 cc.) of physiologic sodium chloride solution may be given by rectum every six hours until the pulse rate is reduced (usually after four to eight doses). The amount should then be reduced to 15 minims (1 cc.), diluted with 1 ounce (30 cc.) of physiologic sodium chloride solution twice a day.

ACETIC ACID MILK FROM THE ACETIC ACID OF THE UNITED STATES PHARMACOPEIA*

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The purpose and the indications for the acidification of cow's milk in infant feeding have been well reviewed recently by Faber.[1]

The usage of milk acidified by acetic acid in the form of ordinary vinegar has been reported.[2] The chief reason for the employment of acetic acid in its natural state, as in vinegar, was due to the apparent harmlessness of this product, as manifested by its dietary usage from ancient times.

Because of the variability in the acidity of different brands of vinegar, only one of about average strength,[3] labeled 5 per cent acidity, was prescribed for use in the home. In this way, a uniform acidification was obtained.[4] Barreled vinegar of tested acidity was used in corresponding proportions for the hospital cases.

U. S. P. ACETIC ACID MILK

Recognizing the desirability of a chemically pure acetic acid of official standard strength, I used the acetic acid of the United States Pharmacopeia in the place of vinegar during the last year. One dram (3.75 cc.) of acetic acid, U. S. P. (36 per cent acid) was added to 15 ounces (450 cc.) of cow's milk, or 1 part of the acid to 120 parts of milk. In the home, 1½ *dipped* common teaspoonfuls of the acid was added to 1 quart of milk. The acetic acid addition to the milk was 0.3 per cent. The hydrogen ion concentration was about p_H 4.8.

In general, the detail of preparation, other than the acid element of the food, and the usage of the mixture were the same as for vinegar acetic acid milk.[2] The milk was previously sterilized and cooled, and the acid was mixed directly with the cold milk. The mixture was only moderately warmed before feedings. Prepared in this manner, the mixture was characterized by fine curds and a creamy consistency.

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* Received for publication, June 10, 1926.

1. Faber, H. K.: Acidified Milks with Special Consideration of the Indications and Limitations to Their Use, Am. J. Dis. Child. **31**:395 (March) 1926.

2. Dunham, B. S.: Acidification of Milk with Vinegar (Acetic Acid) in Infant Feeding, Am. J. Dis. Child. **29**:200 (Feb.) 1925.

3. "Pure Cider Vinegar" and "Distilled White Vinegar," each labeled 5 per cent acidity, were used. Made by H. J. Heinz Company, Pittsburgh, Pa.; Toronto, Canada; London, England.

4. A pint of vinegar acetic acid milk was made from 1 ounce (30 cc.) of vinegar of about 5 per cent acidity to 15 ounces (450 cc.) of cow's milk. This equaled 1 *dipped* common teaspoonful of vinegar to each 3 ounces of milk in the formula.

Corn syrup diluted with an equal volume of water was added in the amount of 1 ounce (30 cc.) of the diluted syrup to the pint (480 cc.) of milk. The mixture was given undiluted, except to infants younger than 2 months who received 4 ounces (120 cc.) of water or gruel in the total daily feeding. Between the tenth and twelfth months of age, the acidity was gradually lessened and discontinued. Four-hour feeding intervals were used.

The cost of the acidulation with acetic acid, U. S. P. (36 per cent acid) at the prevailing retail price of the acid (30 cents per pound) was about ¼ cent per pint of milk, about the same as that from barreled vinegar (30 cents per gallon).[5] With bottled vinegar (57 cents per half-gallon),[3] the cost was about 1 cent per pint of milk.

CLINICAL RESULTS

The clinical results from some fifty infants on the U. S. P. acetic acid milk, for periods ranging from two to eleven months, have been excellent, and comparatively equal to those on vinegar acetic acid milk. In no instance was it found necessary to change the type of feeding. Especially good results were noted in cases of simple malnutrition. The mixture was found to be well suited as a routine food for hospital and dispensary cases because of the constancy of good results and the infrequency of necessary changes of formulas. The food was well liked by the infants from the very beginning and the digestion was good.

In instances of parenteral infection with accompanying diarrhea, the fat and sugar elements of the formula were reduced temporarily without any change of the acid content. Diarrhea attributable to the acetic acid element of the formula was not encountered, but constipation sometimes occurred. An additional amount of syrup, or the more laxative cereals and fruits, were prescribed for constipation when possible.

Cereal gruels were given not later than the third month of age, and vegetable mash was begun at the fifth month. Orange juice and cod liver oil were given as soon as the state of the digestion permitted. Direct sunshine was utilized when available. Under the foregoing management, the rate of gain, the tissue turgor, musculature and color, and the improvement in the appearance and general well-being were satisfactory.

COMMENT

Satisfactory clinical results, equal to those from vinegar acetic acid milk, have been obtained from the acidulation of milk with the chemically pure acetic acid of the United States Pharmacopeia. The acidification was uniform, the preparation of the formula was simple, and the expense of acidulation was small.

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LEAD POISONING IN CHILDREN

WITH NOTES ON THERAPY *

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ETIOLOGY

The manifestations of lead poisoning in children have been described by several writers, and excellent discussions of the etiology and symptomatology are available.[1] Failure to recognize the disease can be attributed to lack of acquaintance with the symptoms, which are in most cases quite characteristic; therefore a brief résumé of the more important points will be of value.

The disease is usually secondary to a perverted appetite. In this condition, which is known as pica (footnote 1, fourth reference), infants and children may ingest sand, coal, cloth, hair and paint, the last chewed from toys, cribs and woodwork. The derangement of appetite may be only habit, or it may result from gastro-intestinal disturbances, intestinal parasites, mental deficiency or neurosis. In any event, pica, in our experience, is the most frequent forerunner of lead poisoning, as it is of relatively common occurrence and may result in the repeated ingestion of small amounts of lead. Weeks may elapse before symptoms arise, and the perversion of appetite is passed over lightly or not mentioned by the parents who have become accustomed to the strange habits of the child.

SYMPTOMS

The essential clinical picture in lead poisoning is an anemia associated with gastro-intestinal disturbances, such as loss of appetite, constipation, abdominal pain and vomiting. The anemia may become quite marked. It is characterized by reduction in the erythrocyte count with the appearance of basophilic stippling in the cells. Anemia may be the only sign in mild cases. Lead colic, as such, is seldom recognized in children.

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* Received for publication, May 27, 1926.

* From the Department of Pediatrics, Harvard Medical School, and the Children's and Infants' Hospitals.

1. Blackfan, K. D.: Lead Poisoning in a Child with Reference to Lead as a Cause of Convulsions, Am. J. M. Sc. **153**:877 (June) 1917. Guerbet: Lead Poisoning from Crystal Nursing Bottle, Bull. Acad. de méd., Paris **80**:149 (Aug. 6) 1918; ibid., Lead Poisoning from Nursing Bottles, Nourrisson **6**:344 (Nov.) 1918. Ruddock, J. C.: Lead Poisoning in Children with Special Reference to Pica, J. A. M. A. **82**:1682 (May 24) 1924. Auerbach, F.: Death of Infant Following Use of Lead Plaster on Breast, Med. Klin. **16**:1037 (Oct. 3) 1920. Historical Account of Occurrence and Causation of Lead Poisoning Among Queensland Children, M. J. Australia **1**:148 (Feb. 11) 1922. Holt, L. E., Jr.: Lead Poisoning in Infancy, Am. J. Dis. Child. **25**:229 (Nov.) 1923.

Loss of appetite and constipation are early and very marked symptoms. Vomiting, often of a projectile type, appears in more pronounced cases. The characteristic lead line, a punctate precipitation of black granules in the gum margin above the incisor teeth, is best seen with a hand lens, and if present is good evidence of lead poisoning. It is a deposit of lead sulphide in the gum margin and does not occur in clean mouths. It is only occasionally present in the disease in children.[2]

In severe cases, neuritis [3] and encephalitis occur. Indefinite pains in the joints and muscles, with weakness of the legs, and reflex anomalies may be early signs of lead polyneuritis.[4] Encephalitis [5] appears, especially in lead poisoning of long duration. It is probable that the frequent occurrence of lead encephalitis in children is due to the fact that the lead is ingested in small doses—a method said to be most conducive to severe poisoning. The signs are variable, and may change rapidly, simulating tuberculous meningitis from which it is often only with difficulty distinguished. Vomiting, headache, stupor and convulsions are prominent features. The prognosis of this severe form of the disease has been considered almost uniformly fatal. Convulsions, frequently repeated, or of several hours duration, are the usual terminal manifestation. The spinal fluid [6] is clear, under increased pressure, and may show a positive test for globulin, a slight increase of lymphocytic cells, or both.

Lead amblyopia,[7] though said to be rare, has been reported with lead encephalitis in children. It arises from neuritis of the optic nerve, and atrophy of the retinal cells. Retinal hemorrhages and papilledema may occur.

TREATMENT

Heretofore, treatment has not been entirely satisfactory. Magnesium sulphate and potassium iodide have been used with some degree of success, as have also the de-ionization baths of Oxley.[8] In lead

2. Littlejohn, E. S.: Three Cases of Lead Poisoning in Children M. J. Australia **2**:63 (July 15) 1922.

3. Fisher: Lead Poisoning with Special Reference to the Spinal Cord and Peripheral Nerve Lesions, Am. J. M. Sc. **51**:54, 1892.

4. Friedberg, E.: Chronic Lead Poisoning in Children, Arch. f. Kinderh. **71**:25 (Feb.) 1922; abstr. J. A. M. A. **78**:1172 (April 15) 1922.

5. Strong, R. A.: Meningitis Caused by Lead Poisoning in a Child of Nineteen Months, Arch. Pediat. **37**:352 (Sept.) 1920. Thomas, H. M., and Blackfan, K. D.: Recurrent Meningitis Due to Lead in a Child of Five Years, Am. J. Dis. Child. **8**:377 (Nov.) 1914. Suzuki, T., and Kaneko, J.: Serous Encephalitis in Infants from Lead Poisoning, J. Oriental Med. **2**:55, 1924; abstr. J. A. M. A. **82**: 1819 (May 31) 1924.

6. Weller, C. V., and Christinson, A. D.: Cerebrospinal Fluid in Lead Poisoning, Arch. Neurol & Psychiat. **14**:327 (Sept.) 1925.

7. Gibson, J. L.: Ocular Neuritis Due to Lead Poisoning, M. J. Australia **2**:201 (Sept.) 1917. De Schweinitz, G. L.: Toxic Amblyopias, Alvarenga Prize Essay, College of Physicians of Philadelphia, October, 1894.

8. Oxley: Electrolytic Treatment of Lead Poisoning, Lancet **2**:848, 1914. Gibson, J. L.: Importance of De-ionization in Treatment of Plumbism in Queensland Children, M. J. Australia **1**:272 (April 5) 1919.

encephalopathies, however, little effect has been obtained from either method. The de-ionization method has been adopted in Australia, where the occurrence of lead poisoning in children was of such importance as to require government action in restricting the use of lead paint.

It is the purpose of this paper to call attention to the unrecognized frequency of the condition, and to detail experiences in treatment. The treatment used in the cases to be presented is that recommended by Aub.[9] The mechanism of absorption, transportation, storage, and excretion of the metal is of the utmost importance, but will be considered only as necessitated in explanation of the treatment.[10]

The mechanism of transportation is similar to that of calcium, and circumstances favoring calcium deposition favor lead storage, and conditions effecting calcium removal likewise affect lead. Symptoms of lead poisoning occur when the metal is circulating in the blood stream, or when bound especially in the liver and brain. It is stored in the bones in an inert form, where it may remain indefinitely without causing symptoms. However, under certain conditions, large amounts of the metal are released into the circulation and then acute symptoms recur. This has been known to happen years after removal from exposure to lead.

In the absence of severe symptoms, especially those of encephalitis, deleading, or the withdrawing of lead from the bones and the hastening of its excretion, may be attempted. This is accomplished by making the lead salts more soluble through the production of an acidosis, together with the maintenance of a diet low in calcium. Alkalosis will also produce lead excretion, but to a less extent than acidosis. Aub has found ammonium chloride acidosis to produce the greatest increase in lead excretion.

As deleading is accomplished by bringing the stored lead into solution in patients severely ill with encephalitis, the procedure becomes dangerous through the possibility of aggravating the condition by adding to the circulating poison. Instead, in those severely ill, the deleading process is reversed, to produce storage of the dissolved metal in the bones. Although a diet rich in calcium, together with careful avoidance of acidosis, may be sufficient to cause amelioration of symptoms, it is advisable to administer calcium salts in large doses. In the severely ill patients with persistent vomiting or convulsions, the oral administration of calcium is either impossible or is so slow in its effect that intravenous therapy is required. For this purpose, from 50 to 100 cc. of 2 per cent

9. Aub, J. C.; Fairhall, L. T.; Minot, A. S., and Reznikoff, P.: Lead Poisoning, Medicine **4**:1-250 (Feb.-May) 1925.

10. For a complete discussion, the reader is referred to the recent monograph of Aub and his co-workers.

solution of calcium chloride are given at daily intervals until the convulsions and other dangerous manifestations have ceased.

A rapid subsidence of the symptoms is due to the removal of lead from the circulation. However, improvement does not indicate that the patient is out of danger, as the metal is stored in the bones and under certain circumstances may be released to enter the circulation again and cause acute symptoms. Particularly is this prone to happen during acute infections. Therefore, as soon as the condition of the child permits, deleading should be instituted. In the low calcium diet necessary during periods of deleading, milk, eggs, green vegetables, and many fruits must be omitted entirely. Thus, in very young children deleading is often not feasable because of the inability to provide a diet lacking in these substances. A diet adequate for older children and satisfactory as far as low calcium content is concerned, may contain meat, liver, potato, rice, tomatoes, corn, bananas and milk-free bread. When for any reason, as in very young infants, such a diet cannot be used, the high calcium diet of milk and vegetables should be continued, so as to maintain storage of the lead in the bones, and the patient should be watched carefully for development of acidosis and resulting acute symptoms of lead poisoning. Even in the deleading process recurrence of symptoms should be watched for. The symptoms of recurrence are vomiting, constipation, or increase in the number of stippled cells in the blood. When these occur, treatment should be stopped or reversed.

Since September, 1923, there have been admitted to the Infants and Children's Hospitals seventeen patients showing symptoms attributable to lead poisoning; five were mild cases, twelve were suffering from encephalopathies. This relatively high incidence indicates that lead poisoning is not uncommon. The twelve cases of lead encephalitis represent 14 per cent of all cases of all types of encephalitis seen in the corresponding period. The histories of three cases of lead encephalitis will be reported in detail.

CASE HISTORIES

CASE 1.—P. K., a white girl, aged 2 years, over a period of one year gradually developed an illness characterized by weakness, anemia, vomiting and constipation. On admission to hospital in December, 1923, she was vomiting after each meal, and was markedly constipated. After several days in the hospital, it was noted that she was eating the paint from the crib. Further history obtained at this time revealed that the habit had been present for months.

Physical examination showed a weak, undernourished, mentally subnormal child. A marked tremor and a lead line were noted in the early part of the hospital stay. The blood picture was a secondary anemia, with marked basophilic stippling of the erythrocytes. There was constant glycosuria, but the blood sugar level and glucose tolerance curve were normal.

Course.—Due to the poor physical condition of the child, deleading was considered inadvisable and the treatment to induce storage was instituted. On a high

calcium diet, improvement was slow, but steady. She gained weight, became stronger and less anemic. After five months she was discharged.

Two months later she was readmitted in convulsions. For five days prior to this admission she had been listless and without appetite. The day before admission she was quite drowsy and had a "fruity" odor to the breath. Convulsions had appeared six hours before admission and continued without cessation until respiration ceased two hours after admission to the hospital. Death was due to respiratory paralysis; the cardiac action continued under artificial respiration for three hours. Urinalysis showed a trace of albumin and positive tests for sugar, acetone and diacetic acid.

The spinal fluid was under increased pressure, slightly cloudy, contained 70 cells per cubic millimeter and gave a positive reaction for globulin. Lead analysis made in Dr. Aub's laboratory showed relatively large amounts in the liver, brain and bones, with less of the metal in the other viscera.

Comment.—This case illustrates the typical onset with pica, followed by anemia, vomiting and constipation; the amelioration of milder symptoms by diet alone; and the potential danger that continues to exist after acute symptoms have subsided. It is thought that in this case an increasing acetone body acidosis contributed to the release of lead from the bones, and the sudden appearance of an encephalitis with fatal termination. The mother had been warned against the child's habit of eating paint, and reported that to her knowledge there had been no nibbling of furniture or woodwork since the previous admission.

The attention is called to the spinal fluid findings, which are typical, and to the incidence of glycosuria. Glycosuria is not reported as part of the picture of lead poisoning but has been present in several of our cases. One cannot say whether this represents diabetes due to damage of the pancreas by the metal or a renal glycosuria. The normal blood sugar and normal glucose tolerance curve suggest the latter, although lead was demonstrated in the pancreas.

CASE 2.—J. S., a white boy, aged 23 months, was admitted to the Infants' Hospital Aug. 30, 1924, because of loss of weight, vomiting and constipation. For nine months he had gnawed at the crib and furniture. Physical examination showed a pale, undernourished child lying in a stupor. Two convulsions occurred on the day of admission. The temperature was elevated to 104 F. Blood examination showed a secondary anemia with marked stippling. The urine contained a trace of sugar. A lead line was present.

Course.—As nothing was retained by mouth, parenteral fluids were given repeatedly throughout the first few days. Convulsions were frequent and the condition of the child was grave. Intensive calcium therapy was instituted, with a view to inducing storage of the metal. The persistent vomiting prevented oral medication, so that calcium chloride was given intravenously. There was rapid improvement after daily intravenous injection of 1 Gm. of calcium chloride in 2 per cent solution. As the convulsions ceased and the stupor lessened, marked irritability appeared. Lumbar punctures with removal of considerable quantities of spinal fluid had a quieting effect at this stage.

There were no convulsions after the first few days of treatment. Later evidences of improvement were cessation of vomiting and diminution of irritability. In the hospital stay of one month, the child had received 10 intravenous injec-

tions of calcium chloride, totaling 15 Gm., and had retained 70 Gm. of the calcium lactate offered by mouth.[11]

When improvement had progressed sufficiently to make further examination possible, it was found the child made no attempt to talk, although he had previously been talking quite well; that objects could not be grasped with the hands, that he could not stand; that hearing was impaired and that he was blind. Examination of the fundi showed what was interpreted as optic atrophy.

Subsequent Course.—After two months at home on a high calcium diet the child was readmitted for a period of deleading. He had improved considerably. The appetite was good, he was gaining weight, the anemia had improved and the weakness of the arms and legs was less marked. He was still quite irritable. Vision seemed to have begun to return and fundus examination showed that the disks were less pale. After two months of a deleading treatment, the child was again discharged. A paresis of the left arm and left leg persisted, for which he continued to receive muscle training.

The patient returned (April, 1926) for another period of observation, now a very active, playful child, well developed and nourished, mentally alert, hearing and understanding well, but only beginning to talk. His appetite was good, the bowels were regular, and there was no vomiting. He still tried to nibble the furniture. The sight and hearing were apparently normal. Examination of the eyegrounds was quite difficult, due to lack of cooperation, but fleeting glimpses of the disks and foveal areas showed nothing abnormal. Weakness of the left arm and left leg continued. The child was quite excitable, with crying spells and occasional attacks of twitching of the left arm.

Comment.—This represents a child with a very severe case of lead encephalitis, complicated by peripheral neuritis, deafness and blindness, in whom the treatment was successful. Improvement has continued steadily, and after nineteen months only slight changes have persisted. There has been only one period of deleading and it is not assumed that the child is free from the metal or that all danger of recurrence of symptoms is past, but by careful observation and cooperation of the parents he has made much improvement; further progress is anticipated. Another period of deleading will be instituted.

CASE 3.—R. H., a white boy, aged 20 months, was admitted to the Infants' Hospital, March 25, 1926, with an illness of three months' duration characterized by constipation, loss of strength, pallor and irritability. For one year he had been biting the window sills and the bars of his crib.

He was an undernourished, pale, restless and very irritable child with occasional muscular twitchings. The respirations were irregular, with periods of apnea. The temperature was elevated to 101 F. The blood showed an anemia with many stippled erythrocytes. Spinal fluid contained only 10 cells per cubic millimeter, but gave a positive test for globulin; a film formed on standing.

11. Calcium lactate was given by mouth instead of calcium chloride, because calcium chloride has been shown by Gamble (Gamble, J. L.; Ross, S. G., and Tisdall, F. F.: Studies of Tetany, Am. J. Dis. Child. **25**:455 [June] 1923; Gamble, J. L., and Ross, S. G.: Ibid., p. 471.) and others to be an acid-producing salt, the chloride ion being absorbed from the intestine in excess of the calcium. If calcium is given intravenously, this objection does not apply. Thus, paradoxically, we might give calcium lactate by mouth to produce storage of lead, by the heightened calcium absorption and calcium chloride to produce deleading by the acid action, more of the acid chloride ion being absorbed than of the calcium.

There was an acetone body acidosis as evidenced by acetone in the urine and in the expired air. Lead was demonstrated in the urine. An intradermal tuberculin test was positive.

Course.—On the day following admission, two convulsions occurred followed by unconsciousness, cyanosis and irregularity of pulse and respiration. Forty cubic centimeters of 2 per cent calcium chloride was administered intravenously, followed by 200 cc. of 10 per cent glucose intravenously, to combat the acetone body acidosis. Calcium lactate was offered by mouth. The next day, although the general condition seemed improved, a strabismus developed. Fifty cubic centimeters of 2 per cent calcium chloride was administered intravenously, and 15 grains of calcium lactate every six hours was continued. Convulsions did not recur, and after a few days vomiting ceased, and solid food was retained. The strabismus disappeared but the irritability persisted. The patient was discharged home April 27 on a high calcium diet, to return when his condition had improved sufficiently to warrant deleading. The parents were requested to try to prevent further ingestion of the metal, and to watch closely for recurrence of acute symptoms.

Comment.—This represents another acutely ill patient with early encephalitis, who showed prompt improvement under glucose and calcium therapy.[12] Attention is called to the many points in the history and physical examination which made the condition difficult to distinguish from tuberculous meningitis, particularly in a child who at this age could be assumed to have some tuberculous focus as evidenced by a positive intradermal test.

Although the child is much improved, he is not out of danger, the lead is stored in the bones and care must be exercised in his management until such time as he can be successfully deleaded.

SUMMARY

Lead poisoning is of relatively frequent occurrence in children. In our cases it has usually been associated with pica or with perverted appetite, which causes the ingestion of lead paint with resulting symptoms of anemia, abdominal pain, constipation and vomiting. In the more severe cases, encephalitis ensues, which is often confused with tuberculous meningitis or other forms of encephalitis. Unless proper therapeutic measures are promptly instituted, lead encephalitis is highly fatal.

The administration of calcium salts—calcium lactate by mouth and calcium chloride intravenously, has been demonstrated to produce prompt alleviation of symptoms. Our experience has confirmed these observations. However, the patient is subject to recurrences of acute symptoms of lead poisoning unless excretion of the lead is effected by a deleading process, best accomplished by production of an acidosis, together with a diet low in calcium.

12. As acetone acidosis definitely aggravates the condition, the intravenous administration of glucose would of itself produce some reduction in severity of the symptoms. It was felt to be of definite value in this case.

MAGNESIUM SULPHATE IN THE TREATMENT OF TETANUS NEONATORUM *

REPORT OF CASE

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Since the introduction of magnesium sulphate into the treatment of tetanus by Meltzer, numerous case reports have appeared in the literature, showing a decided reduction in mortality. Smith and Leighton [1] have recently reported eight consecutive cases of acute tetanus; all of the patients recovered with treatment by tetanus antitoxin and magnesium sulphate.

Bratusch-Marrain [2] seems to be the only one to have reported its use in tetanus neonatorum. Kocher [3] warns against its use in these cases, because of the narrow margin of safety in the prevention of respiratory paralysis. However, he mentions a case of tetanus of the head in a child, aged 3 years, cured by Arndt with intraspinal injections of magnesium sulphate. Abt [4] does not mention it in his "Pediatrics" in the treatment of tetanus neonatorum.

Bratusch-Marrain has reported a series of thirty-six cases of tetanus neonatorum, which occurred at the Kinderklinik in Graz from 1906 to 1923. These he divided into two groups; from 1906 to 1921, or those who did not receive magnesium sulphate, and from 1921 to 1923, those who received the magnesium sulphate. In the first group were twenty-eight patients, only one of whom lived, giving a mortality rate of 96.5 per cent. In the second group were eight patients, seven of whom received subcutaneous injections of magnesium sulphate, with recovery in four, giving a mortality rate of 50 per cent. Holt [5] gives the mortality rate of tetanus neonatorum as being between 90 and 95 per cent. There can be no question as to the part played by the magnesium sulphate in the second group. In these cases, Bratusch-Marrain gave antitoxin both intraspinally and subcutaneously, with two 5 cc. subcutaneous

* Received for publication, June 10, 1926.

1. Smith, C., and Leighton, W. E.: The Treatment of Tetanus, With Special Reference to the Use of Magnesium Sulphate, Am. J. M. Sc. **168**:852 (Dec.) 1924.

2. Bratusch-Marrain, A.: Beobachtungen über den Tetanus Neonatorum, Arch. f. Kinderh. **74**:45 (March) 1924.

3. Kocher, T.: Weitere Beobachtungen über die Heilung des Tetanus mit Magnesiumsulfat, Cor.-Bl. f. schweiz. Aertze **43**:97, 1913.

4. Abt, Isaac A.: Pediatrics, Ed. 1, Philadelphia, W. B. Saunders Company **2**:396, 1925.

5. Holt, L. E., and Howland, J.: Diseases of Infancy and Childhood, Ed. 8, New York, D. Appleton and Company, p. 89, 1922.

injections of a 4 per cent solution of magnesium sulphate. With improvement of the patient the magnesium sulphate was given only once daily, then once every two days. The antitoxin was repeated if necessary. He gave no method for computing the dose, but warned against giving larger doses, because of the danger of producing respiratory paralysis. In two infants in whom more magnesium sulphate seemed indicated because of incomplete control of convulsions, relaxation was produced by giving hydrated chloral by rectum. Issekutz, he said, had proved by animal experimentation that hydrated chloral increases the therapeutic action of magnesium sulphate without increasing the danger of respiratory paralysis.

In tetanus, death occurs during a paroxysm from heart-failure or asphyxia, or is due to exhaustion or to starvation. In infants, it is extremely important to keep up the nutrition. Subcutaneous injections of magnesium sulphate bring about enough relaxation to permit the infant to nurse By reducing the convulsions, the body can in time throw off the combined toxin, and the antitoxin given combine with the free toxin.

CASE REPORT

B. H., a negress, aged 26 days, was brought to the baby clinic Aug. 22, 1925, with the complaint of having a large navel.

The infant was born July 28, 1925, at full term and the delivery was normal. The umbilical hernia had been present at birth. A truss had been put on by the family physician after separation of the cord. The infant had refused to take the breast and had been put on a brand of condensed milk. She was brought to the clinic by an aunt who made no complaint about the general spasticity, but when questioned, said the infant had been all right the first week, then had begun to stiffen and had remained so.

Physical Examination.—The child weighed 7 pounds. She lay flat on her back with all the muscles rigid. The arms were flexed and firmly pressed across the chest; the fingers were clenched and could not be opened without danger of breaking the tendons. The legs were extended and crossed scissors-wise with no motion possible at the hips and knees. The lips were pouting, the jaws stiff with less than half an inch opening between the gums. Respirations were short and rapid. The umbilical hernia was large, but showed no signs of inflammation or suppuration. The ring admitted the tips of three fingers. The infant cried incessantly with a peculiar guttural cry, and the slightest touch seemed to produce pain. She could be picked up and handled like a piece of wood; there was no relaxation at any time.

A provisional diagnosis of tetanus neonatorum was made, and 1,500 units of tetanus antitoxin was given intramuscularly. The food was changed to a lactic acid milk formula. The following day, the visiting nurse reported the condition the same. The temperature was 103 F.

August 25 the mother came to the clinic with the baby, and it was then a full history was obtained. The first symptom she had noticed occurred on the tenth day, when the baby's jaws began to stiffen and she could nurse only when the nipple was placed just within the lips. The baby began to grow stiff all over, cried constantly and had convulsions whenever she was touched. Since the last visit there had been violent vomiting immediately after each feeding. There was no change in spasticity. The temperature was 104 F. The spinal fluid examination was normal.

Ten thousand units of antitoxin were given intramuscularly and magnesium sulphate subcutaneously, the dose being 0.2 Gm. per kilogram of body weight in a 10 per cent solution. Half an hour after the injection the arms began to relax and the baby went to sleep.

The following day the mother reported that for the first time in two weeks the baby had slept all night. She took food from the bottle very well and there was no vomiting. Though the muscles were still spastic, the legs could be uncrossed, the fists opened, and the arms and neck flexed. The temperature was then 103.2 F.

By August 29 the temperature was normal and the infant had gained 5 ounces in weight, but had begun vomiting again. This time 0.5 Gm. magnesium sulphate was given in a 10 per cent solution. This was slightly less than the full computed dose. The vomiting stopped, she could move her arms and legs, and she slept for several hours at a time. Improvement then continued uninterruptedly. Three weeks after the first visit there was no spasticity and she had gained 18 ounces in weight.

SUMMARY

The onset of tetanus was on the tenth day, the infection, no doubt, having occurred through the umbilical cord. The infant received no antitetanic serum until the sixteenth day of the disease. She received a total of 11,500 units of antitoxin. Two doses of a 10 per cent solution of magnesium sulphate were given subcutaneously to control the convulsions. Recovery was uneventful.

CONCLUSIONS

1. The effect of magnesium sulphate in the treatment of tetanus neonatorum is purely symptomatic. It causes the relaxation and control of convulsions which other sedatives have failed to do, thus giving the body an opportunity to combat the disease.

2. It is valuable in the treatment of tetanus neonatorum, because it makes normal feeding possible and stops the vomiting.

3. The action apparently is not cumulative, as the dose can be repeated as soon as the effects of the previous dose have worn off.

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THE THERAPEUTIC VALUE OF HEXYLRESORCINOL IN CHRONIC PYELITIS OF CHILDHOOD*

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Through the courtesy of Leonard, we were able to obtain a supply of hexylresorcinol to try out in the treatment of chronic pyelitis in children. Our clinical material consisted largely of patients who had had urinary infections lasting for months and years, rather than for days and weeks. The group, therefore, is made up of patients very difficult to cure. In this series there were fourteen patients, four with definite anatomic lesions of the urinary tract complicating the pyelitis. The duration of the infection was less than one month in one case, between one and six months in two, one year in three, two years in two, between five and ten years in four, and between ten and fifteen years in two cases.

Bacillus coli was the infecting organism in ten cases, streptococcus in two, staphylococcus in one case, and *Bacillus proteus* in one.

Hexylresorcinol was administered in olive oil to a few patients, but it was more often given in gelatin capsules, each containing 0.15 Gm. of the drug. The moistened capsules were easily swallowed, and were not found in the stools. The dosage varied considerably, the initial dose usually being 0.15 Gm. three or four times in twenty-four hours. If no change was noted in the urine after from seven to ten days, the dose was increased to 0.3 Gm. three or four times daily. In four cases a second increase in dosage was made. The maximal dosage was 0.9 Gm. four times daily for a period of four days. In no instance was hexylresorcinol administered for more than forty-nine days. The drug was given to five patients for a period of one to two weeks; to two patients for from two to three weeks; to three patients for from three to four weeks; to three patients for from four to six weeks, and to one for from six to seven weeks. The details of treatment, including subsequent methenamine treatment, are given in table 1.

An analysis of the fourteen cases shows that in only one did hexylresorcinol bring about sterilization of the urine. This was in a girl, aged 1½ years, who had had an infection with *Bacillus coli* for about a year. She was given 0.3 Gm. of hexylresorcinol four times a day for fifteen days, but there was no change in the bacterial content of the urine. Methenamine was then substituted for seven days, but still there was no change in the bacterial count in the urine cultures. Treatment with hexylresorcinol was again resumed, 0.3 Gm. four times daily being

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* From the Section on Pediatrics, Mayo Clinic.

given for ten days, after which cultures of the urine were persistently sterile (table 2). In none of the other cases were there beneficial results from treatment with hexylresorcinol, in spite of what should have been ample dosage. In two cases the large doses of hexylresorcinol had to be discontinued because of nausea and vomiting. Several patients com-

TABLE 1.—*Results of Treating Fourteen Cases of Pyelitis with Hexylresorcinol and Methenamine*

Case	Sex*	Age, Years	Organism	Duration of Disease, Years	Hexylresorcinol Treatment				Methenamine Treatment	
					Times Daily	Dosage, Gm.	Duration, Days	Urine Culture	Results	Comment
1	♀	9	Bacillus coli	9	4 3 3	0.30 0.45 0.90	21 10 6	+ + +	Failure	Duplication and dilatation of right ureter; nausea and vomiting
2	♀	5	Bacillus coli	1	4 4	0.15 0.30	12 8	+ +	Failure	Treatment discontinued because of abdominal pain
3	♂	12	Staphylococcus	0.25	4	0.15	30	+	Success	Cleared up in 1 week
4	♀	3.5	Bacillus coli	1	3 3	0.15 0.30	9 40	+ +	Success	Cleared up in 3 weeks
5	♀	10	Bacillus proteus	9	4 3 4	0.30 0.60 0.60	7 11 6	+ + +	Failure	Atony of bladder
6	♀	8	Bacillus coli	6.5	3 4	0.60 0.60	6 4	+ +	Success	Cleared up in 3 days
7	♀	14	Bacillus coli	10	4 4 4	0.30 0.60 0.90	7 9 4	+ + +	Success	Cleared up in 10 days
8	♂	15	Streptococcus hemolyticus	14	4 4	0.15 0.30	10 30	+ +	.....	Congenital dilatation of ureter
9	♂	5	Bacillus coli	2	3 3	0.30 0.60	2 9	+ +	Success	Cleared up in 10 days
10	♂	1.5	Streptococcus	6 wks.	3	0.15	7	+	Failure	
11	♀	4	Bacillus coli	2	4	0.15	30	+	Failure	Bilateral pyoureter
12	♀	7	Bacillus coli	1	4 3	0.15 0.30	3 8	+ +	Success	Cleared up in 1 week
13	♀	1.5	Bacillus coli	1	4 4	0.30 0.30	15 10	+ —	Failure	
14	♀	9	Bacillus coli	7	4 4 4	0.30 0.45 0.60	4 4 5	+ + +	Failure	Treatment discontinued because of nausea and vomiting

* In this column, ♀ indicates female; ♂, male.

plained of slight abdominal discomfort, not sufficient, however, to necessitate stopping the medication. The infection was difficult to clear up in four cases because of anatomic anomalies, duplication and dilatation of the right ureter in one patient, dilatation of both ureters in two patients, and atony of the bladder in one patient. The infection in the remaining nine failed to clear up during the time in which the hexylresorcinol was administered.

COMMENT

Henline [1] has recently reported a series of cases in adults, in whom the condition cleared up after from sixty to ninety days of treatment with hexylresorcinol. Brown [2] reports a series of sixty-one cases, in nineteen of which he produced a "cure." The results in these cases he groups under "cure, clinical cure, symptomatic improvement, and no change." The treatment in the acute cases covered a period of from seven to thirty-one days, and in the chronic cases from four to five months. Scott and Leonard [3] report a series of twelve cases of pyelitis in children treated with hexylresorcinol. Eight of these cases were their own, three were from the Blackfan Clinic, and one was described in a personal communication from Gates. The case of Gates must be excluded for reasons given by the authors. The three cases from the

TABLE 2.—*Successful Treatment of Case of Pyelitis with Hexylresorcinol* *

Date of Test 1925	Number of Organisms in 0.5 Cc. of Urine	Methenamine 4 Times Daily, Gm.	Hexylresorcinol, 4 Times Daily, Gm.	Comment
4/30	0	...	...	
5/ 6	Innumerable	1.0	0	0.6 Gm. ammonium chloride also administered
5/10	Innumerable	0	0.3	
5/25	Innumerable	0.5	0	1.0 Gm. ammonium chloride also administered
5/30	100 colonies	0.5	0	
6/ 4	Innumerable	0.5	0	Vomited methenamine and ammonium chloride
6/13	Innumerable	0.5	0	
6/16	Innumerable	0	0.3	
6/20	Innumerable	0	0.3	
6/26	0	0	0.3	
6/29	0	0	0.3	

* A girl, aged 1½ years, infected by Bacillus coli and streptococcus.

Blackfan Clinic can hardly be used, because in no instance was sterilization of the urine accomplished, and in only two instances did the pus disappear from the urine. The remaining eight cases were equally divided between acute and chronic conditions. Four patients had infections lasting four weeks or less, and four had infections which had lasted from one to six months. Three of the acute cases cleared up in two weeks, one and a half months and two months, respectively, and three of the chronic cases required treatment for periods varying from twenty-eight days to three months. The two cases in which hexylresorcinol treatment failed were treated for fifty-four days and four months, respectively. The results in the acute cases can hardly be considered better than what might have occurred in an ordinary case

1. Henline, R. B.: Hexylresorcinol in the Treatment of Fifty Cases of Infection of the Urinary Tract, J. Urol. **14**:119-133, 1925.

2. Brown, D. A.: Hexylresorcinol in Infection of the Urinary Tract. Results in Sixty-Three Cases, J. A. M. A. **86**:668-670 (March 6) 1926.

3. Scott, W. J., and Leonard, Veader: Hexylresorcinol in the Treatment of Pyelitis of Infancy and of Childhood, Am. J. Dis. Child. **31**:241-249 (Feb.) 1926.

of pyelitis treated by alkalization and forcing of fluids for an equivalent length of time.

It is difficult to foretell what would have been the result in my series if treatment had been carried on for two or three months, but it is striking that in six of the nine uncomplicated cases the infection was cleared up by administration of methenamine and ammonium chloride in a relatively short time; in three days in one case, in seven days in two, in ten days in two, and in three weeks in one. In the three remaining cases, treated with hexylresorcinol and methenamine, one urine culture was sterile after all medication had been stopped for one month. The other two were unaffected by any treatment.

What relation the preliminary hexylresorcinol treatment may have had on the rapid clearing up of the infection after the treatment with methenamine is impossible to determine. It must be pointed out, however, that a similar series of chronic cases cleared up without this preliminary treatment. The value of a therapeutic agent for a disease as variable in its course as is acute pyelitis in childhood must be determined by carefully controlled cases. On the one hand, in a small group of cases there may be a large percentage of infections which will not clear up with any form of treatment; on the other hand, there may be a large number of infections that will clear up spontaneously. Therapeutic results to be of significance must be obtained in a large percentage of cases within a time interval that excludes spontaneous healing.

In the chronic cases, there is less difficulty in interpreting results because the condition is more constant. In the case in which the urine did not become sterile under treatment with hexylresorcinol and methenamine and yet cleared up following a month of no medication, the infection had undoubtedly been so reduced by the treatment that it involved only the bladder, as shown by cystoscopic examination, and time completed the cure.

It might appear that the hexylresorcinol treatment was not continued long enough to achieve results. This objection loses its force when the infection, unaffected by two or three weeks' treatment with hexylresorcinol, cleared up in less time after administration of methenamine. When hexylresorcinol was first introduced, it appealed particularly to the pediatrician because it was said to be effective in a solution of alkaline reaction. It seemed to be a valuable addition to the treatment of pyelitis with alkalis and forcing of fluids. Recent work by Leonard and Frobisher,[4] however, indicates that the forcing of water and the alkaliza-

4. Leonard, Veader, and Frobisher, Martin: Surface Tension: The Clinical Significance of a New Factor in Urinary Antisepsis Suggested by Certain Experimental Observations with Hexylresorcinol, Tr. Am. Assn. Genito-Urin. Surg. **18**: 333-340, 1925. Clinical Application of Hexylresorcinol in Urology with Observations on the Significance of Surface Tension in Urinary Antisepsis, J. Urol. **15**: 1-10, 1926.

tion of the urine interfere definitely with the bactericidal action of hexylresorcinol. No alkalis were given to the patients in this series, but no attempt was made to restrict the intake of fluid. If no drug were available to produce results more quickly, the long continued administration of hexylresorcinol would be justified. However, a new drug must measure up to, if not exceed, the standard set by other drugs used in the treatment of a disease.

SUMMARY

In a series of fourteen cases of pyelitis, treatment with hexylresorcinol carried on for a period of from one to six weeks was successful in only one case. In six of nine uncomplicated cases of pyelitis which did not yield to treatment with hexylresorcinol, bacteriologic cure was achieved with methenamine in from one to three weeks.

PROPHYLAXIS OF MEASLES*

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Von Torday,[1] Weaver,[2] and Zingher,[3] have reviewed the literature on the use of convalescent measles serum in the prophylaxis of measles. The number of susceptible subjects injected, and the results, are summarized in table 1.

Tunnicliff and Hoyne[4] injected goats with the green producing diplococcus suggested by the former author as being the cause of measles, and used the serum of this animal in the same way as others use measles convalescent serum.

METHOD OF EXPERIMENT

From Jan. 1, 1923, to April 1, 1925, 190 susceptible persons have been injected intramuscularly with measles convalescent serum as a prophylactic measure, no serum being given when the history of exposure was more than six days. The serum obtained was from donors eight days after the rash began to disappear; was inactivated one hour at 56 C., sealed and stored on ice, no preservative being added. In some of the experiments the serum was from eight to twelve months old and still seemed to be potent. After the injection, the susceptible exposures were not isolated, so that their contacts with measles cases were both definite and frequent. There was no local reaction to the injection. In most instances there was a rise in temperature of from 1 to 1.5 C., beginning within twenty-four hours after the injection, and lasting rarely longer than twenty-four hours. In six susceptible subjects, diarrhea was noted. The results are tabulated in table 2. One hundred and seventy-three susceptible patients were protected, while seventeen developed attenuated measles. No protected susceptible subject developed typical measles.

The cubicle isolation system is used in the contagious division of the Cleveland City Hospital, and the technic practiced is that introduced into this country by Chapin and Richardson of Providence. Neverthe-

* Received for publication, May 19, 1926.

* From the Division of Contagious Diseases, Cleveland City Hospital, and from the Department of Pediatrics, Western Reserve University.

1. Von Torday, F.: Preventative Inoculations in Institutions, Jahrb. f. Kinderh. **103**:307 (Dec.) 1923.

2. Weaver, G. H., and Crooks, T. T.: Convalescent Serum in Prophylaxis of Measles, J. A. M. A. **82**:204 (Jan. 19) 1924.

3. Zingher, A.: Convalescent Whole Blood, Plasma and Serum in Prophylaxis of Measles, J. A. M. A. **82**:1180 (April 12) 1924.

4. Tunnicliff, Ruth, and Hoyne, A. L.: Further Studies in a Diplococcus from Measles; Prevention of Measles by Immune Goat Serum, J. Infect. Dis. **38**: 48 (Jan.) 1926.

TABLE 1.—*Susceptible Patients Injected and Results*

Author	Susceptible Cases Only	Amount of Convalescent Serum Injected Intramuscularly if Length of Time after Exposure Was Less Than 4 Days	If Over 4 and Up to 8 Days	Protected	No Protection, Had Measles	Protection Not Absolute, Had Mild Measles	Per Cent Protection
Von Torday (including Degkwitz' reports): Jahrb. f. Kinderh. **103**: 307, 1923	2,000	.....	.....	..	..	..	97
Weaver: J. A. M. A. **82**: 204, 1924	48	5-10 cc.	.....	44	1*	..	91.6
Zingher: J. A. M. A. **82**: 1180, 1924	102†	2.5 cc.	5-7.5 cc.	93	3	7	90.1
Salomon: Deutsche med. Wchnschr. **49**: 1151, 1923	62	.....	.....	..	..	..	59.7
Kuttner: Ztschr. f. Kinderh. **36**: 119, 1923	225	4 cc. pooled	7 cc.	..	States failures (12.4%) either had slight or typical measles	..	....
Wallgren: Svenska. Läk. Sällsk. Handl **385**: 1924	48‡	.....	.....	..	..	..	....
Pesetke: J. Missouri M. A. **21**: 63, 1924	18	2.5 cc.	5 cc.	17	0	1	94.4
Sinclair and Avery: Mil. Surg. **55**: 697, 1924	80	.....	.....	..	..	..	96.2
Soriceanu: J. A. M. A. **85**: 1258, 1925	2,000	Details not given	.....	..	..	..	96

* In three subjects the rash appeared from one to six days after the serum was injected. In one, the rash came out fifteen days after the administration of serum on the day of exposure.

† One child was protected for twenty-eight days, and developed measles on the forty-second day after a second exposure.

‡ Three fourths of the children treated during the first five days after exposure remained either perfectly well or contracted slight measles without complications.

TABLE 2.—*Results of Injections in 190 Subjects*

Number of Exposures Injected	Length of Time after Exposure, Days	Amount Injected, Cc.	Protected	No Protection	Protection Not Absolute, Mild Measles	Per Cent Protection
Hospital "A"						
9 exposures (1st series).....	2 to 4	2.5 to 5	8	0	1	..
5 exposures (2d series)*.....	2 to 4	2.5 to 5	4	0	1	..
Hospital "B" 9 exposures.....	2 to 4	2.5 to 5	9	0	6 had slight diarrhea	..
Private practice, "A" and "B" combined, 15 exposures.....	2 to 4	2.5 to 5	14	0	1	..
Contagious Hospital, 152 exposures.....	2 to 4	2.5 to 5	138	0	14	..
Total.....190	.....	.....	173	0	17	91
Subsequent injections, various hospitals, private practice, etc.....190	1 to 6	3 to 5	195	0	4	98—
Total.....380	.....	.....	368	0	21	94.3+

* All susceptibles admitted to this hospital for two weeks following the last measles case were injected with convalescent measles serum on admission. The exact number was not known and hence not included.

less, our experiences with measles, chickenpox and smallpox, has been such that, in the past, we have had to consider these diseases separate from the other contagious diseases, and treat them in "ward units," but, with the routine use of convalescent serum, no more attention is paid to measles than to the other contagious diseases. In the pediatric divisions of the other hospitals, where measles serum was used, the wards were not closed for quarantine, new patients were admitted, who were given at least 3 cc. of convalescent measles serum intramuscularly, and epidemics were controlled.

An outbreak of measles in another hospital gave us the opportunity for a well controlled experiment. Patient B. B. came down with measles at hospital "A" on April 3, 1925. In the same ward, one

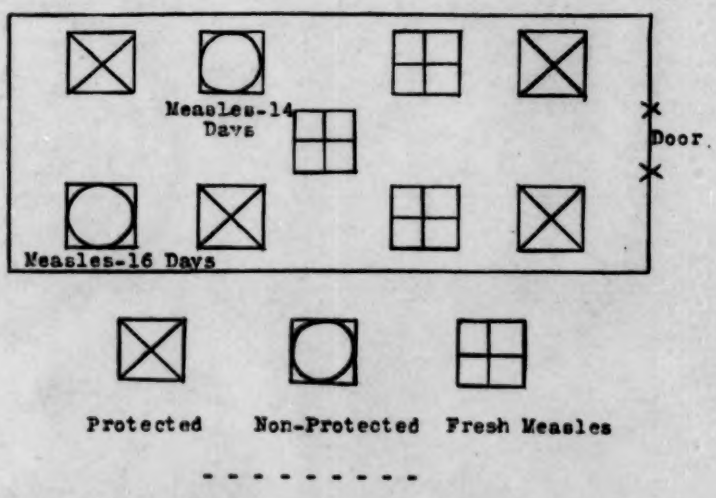

Chart 1.—The arrangement of patients in ward "A."

patient (L. K.) contracted measles on April 15, and another (E. M.) on April 16. Nine days later, on April 24, two more patients (J. F. and J. P.) developed measles. April 26, two more patients (M. G. and G. M.) broke out with measles, and it was decided to transfer the remaining susceptible cases in the ward to the contagious division at the city hospital. There were fourteen cases in this group, all definitely exposed within two days of their admission to the contagious hospital. Eight of these subjects were protected and six were not protected. One of the former group broke out with measles the next day after admission, leaving seven protected and six nonprotected. The nonprotected and protected subjects were mixed with new cases and no personal isolation was practiced. In wards "A" and "B," the arrangements are shown in charts 1 and 2.

Five of those originally protected were grouped as shown in chart 3, and patients with fresh measles were admitted to beds marked with a plus sign. No further convalescent serum was given to these patients. One patient contracted measles after forty days. The others were lost to our control after periods of from thirty to forty-five days. All were seen, the parents were interviewed sixty days later, and there was no history or evidence of measles, but it may be possible that a mild attack could have been present at any time and not have been recognized by the parents.

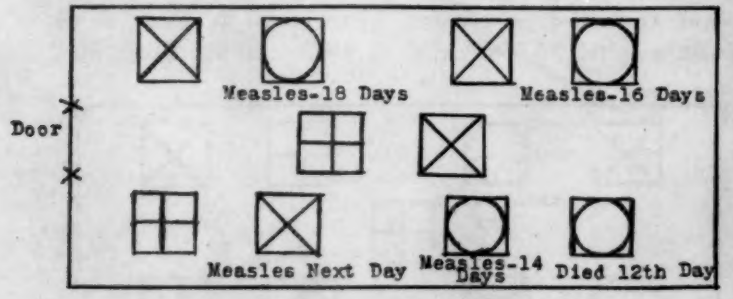

Chart 2.—The arrangement of patients in ward "B."

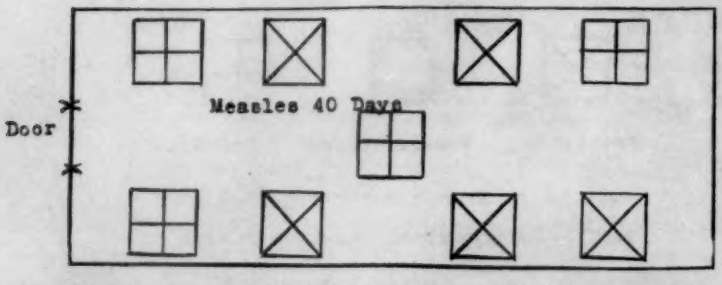

Chart 3.—The arrangement of patients in ward "C." In these wards, all of those nonprotected contracted measles; those protected did not.

In the latter part of 1925 at the contagious and pediatric division of the Cleveland City Hospital, Babies and Children's Hospital, and in the private practice of a few pediatricians, 199 patients exposed to measles have been protected, in only four of whom measles developed.

Due to the crowded condition of the hospital, patients with measles were admitted to three wards with other cases in the usual manner, but strict isolation was ordered. The three wards selected were one above the other. All of those in the middle ward were injected (as was each one subsequently admitted to this ward) with 3 cc. of measles convalescent serum. Each ward has a capacity of thirty-three beds, which are practically 100 per cent occupied at all times. In the protected

ward, no cases of measles developed over a period of forty-five days, notwithstanding the fact that the turnover was twice as fast in this ward than in those on the other two floors. In the latter wards, fourteen cases of measles developed in from fourteen to twenty-nine days, eight cases in the lower ward, which was all the available susceptible material, and six in the upper ward.

The upper ward was then protected. Experience has taught us that not only must the patients present at the time of cross infection be injected, but also each one subsequently admitted. If measles breaks out again, all of those exposed will receive another injection of serum. Measles was stopped in this ward, with only four subsequent cases

TABLE 3.—*Findings in Twenty-One Subjects*

Case	Conjunctivitis	Rhinitis	Bronchitis	Koplik's	Highest Fever	Disease Started	Rash
1	—	+	—	+	101	8 days after	Few macules, face only
2	+—	+	—	+	100	10 days after	Few macules about ears
3	—	—	—	+	98.5	11 days after	None
4	—	+	+—	+	102	6 days after	Scattered macules
5	+	+	+—	+	102.5	5 days after	Scattered macules
6	—	+—	—	+	100	14 days after	Macules, face only
7	+—	+—	—	+	101	45*	Scattered macules over body; disappeared in 48 hours
8	—	—	—	+?	98	15 days after	Macules about ears
9	—	—	—	+	100	16 days after	Macules about face and neck
10	—	—	—	+	99	12 days after	Rash over face and neck
11	+	+	+—	+	102	10 days after	Rash over body; discrete, faded quickly
12	—	+—	—	+	100	8 days after	Scattered maculopapular rash faded rapidly
13	—	+—	—	+?	101	12 days after	Rash, face and chest, scattered
14	—	—	—	+	100	10 days after	Rash was macular
15	—	—	—	+	99	13 days after	Few maculopapules
16	+—	+	+—	+	101	11 days after	Maculopapules, discrete
17	—	—	—	+	99	9 days after	Scattered generalized
18	+	+	—	+	101.5	14 days after	Measles over body; disappeared in 36 hours
19	+	+	—	+	103	14 days after	Typical measles; temperature normal next day
20	—	+	—	+	99	15 days after	Macules about ears only
21	+	+	—	+	101	14 days after	Few macules about face and ears

* This patient in Hospital "A" was probably exposed a second time to an unrecognized case.

occurring from nine to fourteen days later from the original exposures. The lower ward received new admissions, and no protection was given. Every child exposed developed measles, eleven in all, before prophylactic injections were started.

In those injected, the attenuation of measles probably affords the most definite proof of the efficacy of measles convalescent serum. It will be noted (table 3) that thirteen of the twenty-one subjects contracted measles before the usual shortest incubation period of fourteen days—with modifications of the symptoms and signs—and eight only contracted frank measles after fourteen days had elapsed, and this in a modified way.

CONCLUSIONS

1. Three hundred and eighty-nine patients exposed to measles were given from 3 to 10 cc. of convalescent measles serum intramuscularly.

2. Twenty-one of the patients contracted measles, thirteen before and eight after the usual incubation period of fourteen days.

3. In the protected subject, the contracted disease was marked by its attenuation.

MILIARY TUBERCULOSIS IN PREMATURE CHILDREN

REPORT OF TWO CASES *

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CASE 1.—E. H., a colored girl, born July 31, 1924, was admitted to the hospital on September 6, and died on September 20.

Family History.—The father, aged 24, was living and well; the mother aged 20, had had frequent hemorrhages from the lungs since July 15, 1924 (she died on Sept. 17, 1924, of pulmonary tuberculosis). A maternal aunt died of tuberculosis at the age of 20.

The mother was four times pregnant: The first two resulted in two boys, aged 3 and 4 years, both of whom are well; the third, in a miscarriage at the eighth week, and the fourth in the patient at present under discussion.

Past History.—The child was born from six to eight weeks prematurely, but seemed well at birth. The birth weight was unknown. She was fed on condensed milk, one-half teaspoonful in 2 ounces of water every four hours. At the age of 5 weeks she was brought to the hospital because of failure to gain in weight.

Physical Examination.—On September 6 the temperature was 97 F.; weight 3 pounds, 12½ ounces; length, 18 inches; head, 12½ inches; chest, 11 inches; abdomen, 9 inches. Except for prematurity and undernutrition, the infant was apparently normal. The lungs were clear to percussion and auscultation.

Course in Hospital.—The infant was given a diet of relatively high caloric value, consisting of buttermilk, dextrimaltose and water. She took her feedings well, gained slowly for four days, held a constant weight for five days and then lost weight rapidly to 3 pounds 6 ounces on the day before death, thirteen days after admission. On admission, the infant's temperature was subnormal, but on the following day it rose to 100.4 F., fluctuated between 97.5 and 100.5 for two days and then remained normal for two days. No cause for this elevation of temperature could be found. After the short, afebrile period the temperature again rose and then varied between 99 and 103.5 until death. The child gradually became weaker and died on September 20.

The clinical diagnosis was prematurity.

Necropsy Report.—Caseous mediastinal and peribronchial glands. Caseous pneumonia, left lung. Miliary tuberculosis, lungs, liver, spleen and kidneys. Prematurity.

CASE 2.—L. B., a white boy, born Sept. 16, 1925, was admitted to the hospital on October 14, and died November 15.

Family History.—The father, aged 40, was living and well; the mother, aged 36, was ill (she died of pulmonary tuberculosis on November 5).

The mother was six times pregnant. All of the children except this patient, are said to be well.

Past History.—The patient was born from four to six weeks prematurely, but seemed well at birth; the birth weight was 4 pounds. He was nursed for three days, then weaned and fed on a milk, water and sugar mixture at irregular intervals. Because of failure to gain in weight and because the mother

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* From the Department of Pediatrics, Johns Hopkins University, and the Harriet Lane Home, Johns Hopkins Hospital.

was ordered to a state tuberculosis sanatorium for treatment, the child was brought to this hospital for regulation of diet.

Physical Examination.—October 15 the temperature was 97 F.; weight, 4 pounds 2 ounces; length, 18 inches; head, 12½ inches; chest, 10½ inches; abdomen, 9½ inches. Except for prematurity and undernutrition, the infant seemed to be normal. The lungs were resonant on percussion and no adventitious sounds were heard on auscultation.

Course in Hospital.—The infant was given a diet of milk, sugar and water, in sufficient amount to furnish 200 calories per kilogram of body weight. The weight increased 8 ounces during the following week and then remained constant until just before death. Three days after admission, on October 17, the temperature rose to 101 F. and then fluctuated between 99 and 103.5 until the time of death. On the fourth day after admission, October 18, blood and mucus appeared in the patient's stools and a tentative diagnosis of dysentery was made, but no dysentry bacilli could be cultivated from them. The next day diarrhea was noted, seven very fluid stools were passed. This diarrhea persisted until death, becoming even more marked in the last few days of the patient's life. The blood was present for three or four days only. On November 7, the child's diet was changed to whole buttermilk but the diarrhea was not affected. From October 20 to 23 the child vomited frequently and not afterward. Acute otitis media developed on November 6, but incision, drainage and irrigations did not affect the fever. A subcutaneous abscess developed on the right buttock on November 9; this was incised and drained, healing quickly. Staphylococci and *B. coli* were cultivated from the pus obtained. On November 10, the child began to refuse his feedings. He became progressively weaker, lost weight rapidly and died on November 15.

The clinical impression was prematurity and dysentery.

Necropsy Report.—Caseous mesenteric lymph glands with miliary tuberculosis of spleen, liver, pancreas, thyroid and kidneys and tuberculous ulcerations of the jejunum, ileum and colon.

COMMENT

These two cases of miliary tuberculosis are reported for several reasons: first, the rapid course of the disease; second, the absence of clinical symptoms and signs on which to base a diagnosis during life; third, miliary tuberculosis is very rare in infants under 2 months of age, and fourth, the infrequency of this disease in premature children.

In neither case was a tuberculin test done, as it was thought that tuberculosis was so rare in premature children that such a test was not indicated. However, in view of the cases here reported, it seems advisable to urge strongly the use of routine intracutaneous tuberculin tests in premature children, born of tuberculous mothers; in very young children who fail to gain weight on an adequate diet, and in premature and very young children with persistent and unexplained fever. Furthermore, in the second case, the possible rôle of tuberculous ulcerations of the intestines in the causation of severe and long-continued diarrhea, nonamenable to the usual dietary treatment, is well shown.

PROGRESS IN PEDIATRICS

WHAT CONSTITUTES MENTAL HEALTH IN CHILDREN?*

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INTRODUCTION

The task of plotting the limits of normal behavior is not a simple one. I am somewhat heartened by the reflection that the boundaries which have been drawn by others are certainly elastic and flexible. A noted psychiatrist compared the play-behavior of a group of children, who were in a mental hospital because of behavior disorders following epidemic encephalitis, with the conduct of children in Rittenhouse Square, and was able to award the former the more favorable opinion. Rittenhouse Square is where the sons and daughters of Philadelphia's élite disport themselves. The normal child has been called a polymorphous pervert, and has been accused of playing the primary rôle in the grim tragedy of Oedipus Rex, and still he has survived. It is unlikely that anything I may say can injure his somewhat spotted reputation.

CRITERIA OF BEHAVIOR

To be intelligible, I must have some objective criteria. Personality is a highly elusive quantity, but it needs to be seriously considered, since we are forced to measure it by behavior. In other words, and with certain exceptions, when the conduct of a child consistently and actually falls within normal or average limits, then it may be taken to be the expression of a basically sound personality, while, on the other hand, if the personality is distorted or sick, it will give rise to abnormal action which either reveals or attempts to conceal abnormal thought and mood.

How is personality developed? The limitations of this paper forbid anything more than an attempt to expose a limited cross-section of this complex and intricate growth. Whatever more it may be, the child is certainly a sensorimotor mechanism. Like an animal it is stimulated by sensory impressions, and like an animal it gives forth a response. However, the animal is capable of only a limited set of experiences, and it

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* Read before the Annual Meeting, American Child Health Association, May 19, 1926.

is likely that they remain discrete and isolated. The behavior is quite simple. In the child, the experiences are infinitely greater in number and more complex in type. Furthermore, they are rapidly connected, and associated with each other so that responses soon take on a most elaborate and intricate character. Thus a kind of mental pattern, which has numerous by-paths, intercommunications and recesses, is soon wrought and this pattern in some sense molds the personality.

It is futile to judge behavior without reference to environment. Often as I listen to a dramatic recital of the "terrible" and "awful" things which this or that child does or says, my mind is engaged in a consideration of the surroundings in which the particular child breathes and moves and lives. What are its assets and its limitations; its opportunities and its deficits; its sins of commission and its crimes of omission? Does it leave no choice, and make so-called abnormality the only logical and possible response? If it does this, then the conduct is not intrinsically pathologic. No true scientist would be guilty of reporting the behavior of a laboratory animal without allowing for the characteristics of environment, and yet children are expected to tread on a standardized highroad even though the conditions and circumstances of their surroundings have effectually barred and sealed its entrance! When I attempt to sketch an outline of average behavior, you will have in mind that I am assuming the existence of an environment which is at least potentially accessible in the right direction, and capable of furnishing the needed ingredients in something near the correct quantity and quality.

THE LIMITATIONS OF AVERAGE BEHAVIOR

What then may we expect from a child who is not doomed by reason of a badly tainted ancestry, and who is placed in a satisfactory environment? One of the earliest tokens of the inherent stability of the nervous organization is the desire for and the execution of physical motion on the part of the infant. Here is the opportunity to acquire new, pleasurable and varied sensory experiences, and to establish suitable responses. So imperative is this phase of development that its absence or very considerable reduction will not only halt mental growth, but will even impede or prevent the establishment of organic connections in the central nervous apparatus. If no physical reason exists, then a marked reduction of motor movement is somewhat indicative of defective mental health.

To watch a group of children at play is to know at once how potent is imitation in the acquirement of mental soundness. In the playing of "house" or "school," which are historical childhood games, almost the entire play structure is supplied by the imitative faculty. The things the parent or teacher does or says, the way in which they wear their clothing, their mannerisms, and even the very inflections of their voices

are faithfully portrayed. Long before the elaborated play period, the normal child has acquired vocal language largely through a process of imitation. If a child who is not too greatly handicapped physically does not to some extent repeat or essay to repeat the happenings in the immediate environment, then the mental health of that child comes into question. When the behavior content is consistently a thing apart, and has no counterpart in the environment, then one may begin to think in terms of distorted personality, various odd, eccentric and bizarre behavior traits which may even progress to that terrible psychosis—dementia praecox. You may object that child genius is often above and beyond imitation of environment, and my reply would be, "Yes, genius and potential mental disease—they are very similar."

The trait which has been named suggestibility is an indirect, refined and subtle form of imitation. The boundary line between normal and abnormal territory is here very broad, but two extremes exist which are at least the precursors of the pathologic. The first involves an almost total resistance to external influence, and constitutes a real inability to accept any influences flowing from the environment. It is the prototype of the strange negativism of dementia praecox. The second extreme is the constant and abnormally easy acceptance of every suggestion, so that the child behaves like a delicately adjusted weather vane. Its pure expression is to be seen in adult hysteria. Unfortunately, the adequate amount of suggestibility is not measurable, but its pathologic deviation in either direction is fairly obvious, and no psychologic tape measure is needed.

Curiosity is obviously such a common and essential trait that it is the heritage and possession of all children, with the possible exception of the idiot. Qualitatively, it is a sign of normality, but it is naturally extremely difficult to decide when it is beyond the limits of mental health, either in the direction of excess or deficit. Almost every male parent, when he is the subject of a merciless barrage of questions from his offspring, believes that the child is abnormally curious. Almost never is he right. I do not believe I have ever seen a child whose curiosity was so excessive that it could be labelled pathologic. On the other hand, the child who does not pass through the questioning phase, and apparently cannot be stimulated to want to know, and seems unable or unwilling to take any steps to acquire bits of information is probably not well balanced in his growth.

The general assumption concerning the abnormal nature of sex curiosity is so erroneous that it should be given particular mention. Usually children are more curious about sex than about other matters, simply because sex has been attractively clothed in mystery. One does not face the question as to whether sex curiosity is to be satisfied or not. The real question is, will it be satisfied in a natural and constructive

manner, or is the child to be left to tap every available and harmful source of information? Such behavior as the inspection of his own or the sexual organs of other children is not a morbid phenomenon under the usual circumstances. I am inclined to believe that unless the conditions are quite exceptional, the absence of any sex interest during childhood is an extremely dangerous characteristic. Naturally, sex curiosity may become so excessive and concentrated that it passes normal bounds, but, as often as not, the responsibility is in the environment rather than in the child.

There is a trait called the love of power which, in every day, common sense psychology amounts to a desire to be able to control the environment, chiefly for purposes of personal satisfaction. It is not a strange phenomenon in adult life and it has its roots in the days of childhood. All normal children love power; they like to hold the center of the stage. This is not at all remarkable, since in infancy a child is able to control immediate surroundings to a considerable extent. Everyone tried to anticipate the needs and desires of the baby.

However, there comes a time when the child can no longer have its own way, and must begin to conform to the wishes and rights of others. It is not an easy matter to know just how much difficulty the normal child should experience, and manifest by behavior, in the relinquishment of infantile power. In some children the struggle is obvious and is almost entirely on the surface; in others the little tragedy is hidden from adult eyes. This much we do know: A certain amount of love of power is natural and normal; its necessary sacrifice entails some degree of suffering on the part of the child; objective demonstration of the unwillingness to abandon power and be relegated to the commonplace background of conformity to social demands is to be expected from the normal child, but finally, absolute inability to make this compromise and adjustment, as revealed by conduct which by its very persistence rather than by its nature becomes antisocial, is one of the criteria of failure to attain mental health.

Practically all normal children pass through a phase of savagery and romancing. Then they want to run away from home and kill Indians, and they tell tales which would have added to the fame of Baron Munchausen. They are merely stages in normal childhood development, although their manifestations are commonly and erroneously regarded as abnormal.

Freudian psychologists regard savagery as one of the phases which the child recapitulates in the enactment of the condensed, but vivid drama of the evolution of the human animal from primal to civilized behavior. Such discussion is not within the scope of this paper. In attempting to delineate the limits of childhood normality, I should have to say that complete or striking absence of what is commonly designated

"animal spirits" must raise a grave doubt. As a practical point, absence of any degree of the competitive spirit in the games of children makes the issue doubtful. Life is life, and must be judged by the standards of the age in which we live. The veneer of civilization, which we have been at such pains to apply, is still pathetically thin and often wears through. There is still the grim struggle for existence. The child who feels no thrill in victory will have difficulty in finding a place in the world of reality. The very artificiality of his position will often condition an intolerable situation, from which abnormality offers an easy escape into unreality.

I regard romancing in many instances as evidence that the imagination is beginning to grow. Frequently, it helps to quiet the gnawing unrest of a sense of inferiority. In this case, it in itself may not be abnormal though the inferiority may be. In short, it is perhaps fair to say that savagery and romancing which come to the surface in such bizarre and fantastic word and deed are not proof of mental ill health. Their persistence long beyond the usual period is a matter which needs careful investigation.

With certain limitations, intellectual capacity is capable of fairly accurate measurement. Here again, academic rigidity is the hallmark of ignorance of true childhood psychology. Mental defect is a very different thing from mental retardation. The latter is a condition of intellectual backwardness which is conditioned by some handicap either in the body of the child, in his environment or in his emotions. It is recoverable. True mental defect is hopeless. It is an anatomic failure or an early cessation of the brain growth, and just as he who is blind cannot be expected to see, neither can the child who does not have sufficient cerebral capacity be expected to put forth a normal amount of intellectual energy.

He who feels that he can casually give judgment concerning the normality or abnormality of the moods or emotional life of a child is indeed courageous! It is the valor of ignorance. The widest latitude is an everyday occurrence, and inconsistency is the rule. To find a prototype of the mood variations in normal children, I am forced to go to mental disease in adults. The intense psychomotor activity of acute mania is usual in the play of normal children. The profound depression of acute melancholia is not uncommon. It is remarkable how time tempers memory, and the adult who is constantly sighing for a return to the golden days of his childhood seems to have no recollection of its grim tragedies. Even the mood disharmony of dementia praecox, with its odd contrast between feeling, thought and behavior, and the retirement from the world of reality, may be found in normal children. I should say this much of the complex riddle of the emotional life of childhood: If the stimulus or cause of the mood disturbance is such as

is commonly reacted to by average children, then the behavior expression, however strange it may seem, is not definitely abnormal. Finally, and more important, the normal mood life of a child is marked by its flexibility. When we find rigidity and undue persistences, then we have a deviation which is serious.

I presume that something ought to be said in reference to the appreciation of moral values as a mark of normality. Those who are pessimistic would be inclined to say that the moral standards of the age in which we live do not furnish a very satisfactory criterion. It is true that the tendency to disregard the law, which seems to be abroad on every side, does not always constitute a healthy example for children to follow. In judging normal moral reactions we must accept the criteria which we have encouraged directly and indirectly, even though we continue to strive for betterment. In other words, we cannot expect to receive more than we give. Here we have a rather shifting standard, with a fairly firm foundation of instinctive moral sense and a more or less shaky superstructure made up of tradition, custom and present day conventions. This much seems clear. The major portion of moral sense must be acquired, and imitation and suggestibility are the chief routes available for children. If the environment furnishes in fair quantity constructive moral material, not by precept but by example, and it is constantly rejected by the child, then there is a strong suspicion of badly balanced mental health. Naturally, moral deviation may be influenced by such inherent factors as heredity, or by such accidental ones as epidemic encephalitis ("sleeping sickness") or severe head injury.

COMMENT

In this incomplete picture of the child who is healthy in mind, I realize that I have only scratched the surface. For instance, such a primary instinct as self-preservation is so obviously a part of all living organisms that its absence in the child is always pathologic. Again, normal personality was not discussed in any detail. Personality is the sum total of all previous experiences, and the responses to them and its growth are somewhat dependent on the presence and health ultilization of the psychologic traits which have been mentioned.

To build a theoretic composite child, who is sound mentally, one should be able to use rubber as the main ingredient. The chief quality of such a composite needs to be elasticity and flexibility, since to meet the requirements of individual perfectly normal children, a great deal of pulling, bending and pushing is imperative.

However, there should be included the ability and the desire to move, a certain readiness and willingness to imitate, some response to suggestion, a strong leaven of curiosity, an appreciable love of power, a dash of savagery and a seasoning of romancing. There should be intelligence

enough to bring out these traits; enough emotional virility to impress the lessons which they teach, and moral judgment to act as a kind of partial check. The marked diminution of these characteristics is a much safer measure of a sick mind than is their excess.

The final measuring rod is the ability to pass through the critical phases and make adjustments somewhere within the average time limits. The greatest tribute I can pay the child is to view him in the light of his adjustment-accomplishment record. Think of how varied and intricate are the adjustments which many children make! How increasingly complex these adjustments become year after year! To mention only a few of them is to outline a gigantic task. There are the organic adjustments, feeding, bladder, bowels, etc. Constant revision is demanded. Soon must come the surrender to the requirements of civilization in the matter of clothing, property right and in innumerable other directions. Then the upheaval produced by school life or by the advent of a new baby in the household, and the countless accidents and conditions of life, all insisting that the ego be suppressed for the benefit of a larger unity. Then all the finer moral demands have to be placated. Finally, an entirely new set of love experiences are set into motion and they require an effacement of infantile and early childhood love life. Fortunately, there is a strong natural pull in the direction of successful adjustment making. The goal is the right to live mentally and physically in the actual and concrete world; to share in its rewards, pleasures and disappointments. Let us not forget, however, that there is at least a potential pull in another direction, away from the making of adjustments. The punishment for this course of action is to have to live mentally and perhaps physically in a world of unreality. Here, one is not permitted to play an active part in the game of concrete life, but there may be certain compensations—notably an absence of responsibility. After all, a true sign of mental health is the willingness to pay the price which one must pay before being allowed actually to live!

EPILEPSY IN CHILDHOOD*

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Idiopathic or essential epilepsy is a chronic disease of the nervous system characterized by periodically recurring convulsions, lapses or abnormal mental states occurring in persons with a personality defect or constitutional inferiority but with no demonstrated pathologic lesion.[1] It is estimated that 0.4 per cent of the population is epileptic. The personality defect or the "psychobiologic feature" has been demonstrated by Clarke in his excellent monograph, Clinical Studies in Epilepsy.[2] This constitutional inferiority is probably an inherited defect (rather than congenital).

The hereditary predisposition has long been considered a factor in the etiology of epilepsy.[3] The accompanying table gives the variations in statistics on the influence of heredity.

Variations in Statistics on Influence of Heredity

Author	History of					
	Epilepsy, Per Cent	Insanity, Per Cent	Alcoholism, Per Cent	Nervous Instability, Per Cent	Syphilis, Per Cent	Migraine, Per Cent
Spratling [4]	16	7	14	..	..	..
Turner [5]	37	4.8	4	..	..	..
Déjerine [6]	21.2	16.8	51.5	..	..	..
Binswanger [7]	11	29.6	22	..	..	..
Peterman [8]	9	5	2	14	3	21

It must be remembered that a reliable history is extremely difficult to obtain from an epileptic or from his parents. Also, the statistics will vary greatly in different countries and in different centers of popu-

* Received for publication, June 19, 1926.
* From the Milwaukee Children's Hospital.

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2. Clarke, L. P.: Clinical Studies in Epilepsy, Utica, N. Y., State Hospitals Press, 1917.

3. Clark (footnote 2). Gowers, W. R.: Epilepsy and Other Chronic Convulsive Disorders, J. & A. Churchill, 1901. Eccheverria: Epilepsy, New York, William Wood & Co., 1870. Reynolds: Epilepsy, London, 1861. Oppenheim: Textbook of Nervous Diseases, 1911. Finkh, J.: Arch. f. Psychiat. **39**:820, 1903.

4. Spratling: Epilepsy and Its Treatment, Philadelphia, W. B. Saunders Company, 1904.

5. Turner, W. A.: Brit. M. J. **1**:733 (March 26) 1910.

6. Déjerine, quoted by Turner (footnote 5).

7. Binswanger, O.: Epilepsie, in Eulenberg's Real Encyclopedia der gesamten Heilkunde **4**:547 (1908).

8. Peterman, M. G.: Ketogenic Diet in Treatment of Epilepsy, Am. J. Dis. Child. **28**:28 (July) 1924; and an article to be published.

lation. In a consideration of the possibility of inherited characteristics, it is well to consider Maud Slye's emphasis on the definition of heredity.[9]

The character of the disease, the usual progressive degeneration and the constitutional defect classify epilepsy with the heredofamilial degenerations or abiotrophies in which it is also often difficult to obtain a definite family history of disease of the nervous system. Alford says:

> The conditions which most closely resemble epilepsy are clearly the heredofamilial degenerations or abiotrophies. These generally show the influence of heredity, they are acquired, progressively increase in severity, and are organic in nature. Moreover, they are numerous and are particularly likely to affect the nervous system. No other type of pathological process than that here active so closely conforms to the accepted facts about epilepsy. . . . In epilepsy the chief functional involvement may be considered extrapyramidal in type. This motor feature can be plausibly regarded as in series with the tremors, chorea, athetosis, the incoordination and the hypertonus found in various of the other abiotic conditions. A defect permitting convulsions would not be different in principle from one resulting in chorea, athetosis, and other extrapyramidal disturbances.[10]

While the heredity cannot always be so clearly traced as in the families of Block,[11] Rolder [12] and Yawger,[13] it is nevertheless probably always a factor.

The etiology of idiopathic or essential epilepsy remains in obscurity and the diagnosis is still made by exclusion. Given a predisposition to epilepsy by heredity, other factors are necessary for the development of the disease. Congenital abnormalities, cerebral hemorrhage or injury, hydrocephalus, syphilis or acute infectious diseases may produce the irritation necessary to inaugurate the convulsions. These factors may also produce convulsions simulating epilepsy; they should not, however, be considered causes of epilepsy since they produce definite organic lesions of the brain which can usually be demonstrated.[14] In idiopathic epilepsy no definite pathologic lesion has been consistently demonstrated as the basis of the symptoms.[15] (The special and organic forms of

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9. Slye, Maude: Some Misconceptions Regarding the Relation of Heredity to Cancer and Other Diseases, J. A. M. A. **86**:1599 (May 22) 1926.

10. Alford, L. B.: M. J. & Record **122**:340 (Sept.) 1925.

11. Block, E. B.: Tice's Practice of Medicine **10**:407, Hagerstown, Md., W. F. Prior, 1921.

12. Rolder, J. W.: Nederl. Tijdschr. v. Geneesk. **2**:1548 (Oct.) 1925.

13. Yawger, N. S.: New York M. J. **116**:334 (Sept.) 1922.

14. Krumholz: J. Nerv. & Ment. Dis. **40**:17 (Jan.) 1913. Lucas and Southard: Boston M. & S. J. **166**:323 (Aug.) 1912; ibid. **169**:341 (Sept.) 1913. Tilmann: Arch. f. klin. Chir. **92**:496, 1910.

15. Alzheimer: Monatsch. f. Psychiat. u. Neurol. **4**:345, 1898; Centralbl. f. Neurol. u. Psychiat. **27**:497, 1904; Allg. Ztschr. f. Psychiat. **46**:418, 1907.

epilepsy are not considered in this résumé but may be found in the literature.[16] The "abnormal looking brains,"[17] the microscopic findings in certain cases, as hemorrhage, atrophy,[18] degeneration,[19] etc.,[20] the residuals of acute infections[21] are reported in unselected cases.[22] The pathologic findings reported in idiopathic epilepsy may well be considered the result rather than the cause of the disease.[23]

The differential diagnosis of the convulsions of infancy and childhood demands great care.[24] The great majority of epilepsies have their onset before 20 years of age[25] and perhaps over half begin before 15.[26] Epilepsy may begin at any age, but it is not common before the first year. The so-called "teething spasms" and reflex convulsions attributed to fright or emotional disturbances,[27] to phimosis, adenoids and polyps,[28] peripheral nerve lesions,[29] and to worms,[30] can often be explained on the basis of spasmophilia, the most common cause of convulsions in infants between 8 and 24 months of age. Strangely enough, the spasmophilic patients, who transmit their neuropathic diathesis through heredity, seldom develop epilepsy. The early convulsions in infancy[31] may be the first convulsions of epilepsy even when there is a long interval until the next seizure.

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16. Jackson, H. J.: Wood's Monographs **6**:723, 1890. Koschevnikow: Neurol. Centralbl., Dec. 17, 1893. Orlowski: Neurol. Centralbl. **15**:526, 1892. Choroschko: Neurol. Centralbl. **27**:279, 1908. Clarke, L. P., and Prout, T. P.: Am. J. Insan. **54**:185, 1902. Lundborg: Die Progressive Myoclonus Epilepsie, Upsala, 1903. Bourneville: Arch. de neurol. **1**:69, 1880. Bourneville and D'Olier: Ibid. **1**:213, 1880.

17. Thom, D. A., and Southard, E. E.: Rev. Neurol. & Psychiat. **13**:471, 1915.

18. Onuf, B.: Some Interesting Autopsy Findings in Epileptics, J. A. M. A., **44**:1325 (April 29) 1905.

19. Lafora, G. L., and Glueck, B.: Contribution to Histopathology and Pathology of Epilepsy, Gov. Hosp. Insane Bull., Washington, D. C. **3**:98, 1911.

20. Chaslin, P.: Arch. de méd. expér. et d'anat. path. **3**:305, 1891. Hirsch, E.: Med. Klin. **21**:48 (Jan. 11) 1925.

21. Marie, Piérre: Progrès méd., 1887, p. 333.

22. Jacquin and Marchand: Encéphalie, 1913, p. 205. Sioli: Arch. f. Psychiat. **1**:30 (May) 1913.

23. Kasak, M.: Arch. Neurol. & Psychiat. **5**:645, 1921. Popea, A., and Vicol, A.: Compt. rend. Soc. de biol. **93**:747 (Aug. 14) 1925.

24. Peterman: Wisconsin M. J. **25**:181 (April) 1926.

25. Gowers (footnote 3, second reference).

26. Spratling (footnote 4). Turner (footnote 5).

27. Gowers (footnote 2, second reference). Starr: Organic and Functional Diseases, 1913, p. 823.

28. Levinstein, O.: Arch. f. Laryngol. u. Rhinol. **22**:167, 1914.

29. Feré, C.: Les Epilepsies, Paris, 1890.

30. Martha, A.: Arch. gén. de méd., 1891, pp. 513 and 699.

31. Patrick, H. T., and Levy, D. M.: Early Convulsions in Epileptics and in Others, J. A. M. A. **82**:375 (Feb. 2) 1924.

The site of origin of epileptic convulsions remains unsettled. Gordon states:

> Any section of the brain possesses epileptogenous properties and the mechanism of epileptic convulsions lies fundamentally in the disturbed function of the cortical motor cells, the impulses of which are influenced by morbid foci in any region of the intracranial tissue. In Jacksonian epilepsy the site of the lesion must not necessarily be in the motor area itself.[32]

Oppenheim, Munk, Schaefer, Fritsch and Hitzig, Franck and Pitres, Bechterew and others placed the epileptogenous center in the cortex and were of the opinion that clonic convulsions could occur only with the motor cortex intact. Recent experiments by Pike and Elsberg [33] support the newer school, Nothnagel, Luce, Ferrier, Corville, Durat, Pollock, Gordon and Holmes, who maintain that the cortex is not essential for the production of "epileptic" (clonic) convulsions. Pike and Elsberg performed a large number of experiments on young and adult cats. After excision of one or both motor areas and a return of good locomotor reactions, they injected absinthe intravenously, producing tonic and clonic convulsions of the limbs. This work supports the theory of Nothnagel [34] that the medulla and pons may be the epileptic centers. Pollock and Treadway [35] found in decerebrate animals that the medullary symptoms preceded even the aurae. Hence Pollock was led to believe that the medulla and pons were the epileptogenous centers.[36]

The immediate cause of the epileptic convulsion, the factor that provokes the end-result or explosion, is probably a disorder of metabolism, possibly a shift of the acid-base equilibrium to the alkaline side.[37] The tendency to alkalosis is not the only factor since this may occur without provoking a convulsion.[38] Between attacks the neutrality regulation [39] and the general metabolism seem to be normal.[40]

The disturbance of calcium metabolism in epileptics, stressed by French observers (Bigwood [41] and others) may well be a secondary

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32. Gordon, A.: J. Nerv. & Ment. Dis. **61**:142 (Feb.) 1925.

33. Pike, F. H., and Elsberg, C. A.: Am. J. Physiol. **72**:337 (April) 1921.

34. Nothnagel, H.: Epilepsie, in Ziemssen's Cyclopedia, New York, **14**, William Wood & Co., 1877.

35. Pollock, L. J., and Treadway: Arch. Int. Med. **11**:445, 1913.

36. Pollack, L. J.: Arch. Neurol. & Psychiat. **9**:604 (May) 1923.

37. Peterman, M. G.: J. Diet. Adm. & Therapy **4**:23 (Jan.) 1926. Rafflin, R., and Claude, H.: Compt. rend. Soc. de biol. **92**:1361 (May 22) 1925; ibid. **92**:1429 (May 29) 1925, and an article to be published. Haig, A.: Neurol. Centralbl., 1888.

38. Rafflin, R.: Compt. rend. Soc. de biol. **92**:1429 (May) 1925.

39. Jensen: Hospitalstid. **68**:715 (July) 1925. Peterman, M. G.: To be published.

40. Peterman (footnote 37, first reference). Talbot, F. B.; Hendry, M., and Moriarity, M.: Am. J. Dis. Child. **28**:419 (Oct.) 1924.

41. Bigwood, E. J.: Compt. rend. Soc. de biol. **90**:59, 1924.

factor, as a result rather than a cause. The mineral metabolism is dependent on the hydrogen ion concentration of the blood.[42] The effect of the parathyroid glands on the mineral metabolism may soon be definitely established.[43] Such observations as a cholesterolemia,[44] especially during frequent convulsions, are the results of a general disturbance in metabolism.

It has not been scientifically established that the endocrine glands play any part in the causation of epilepsy; therefore treatment on this basis is not justifiable.

The German designation "ovariellen epilepsie" adds only confusion to the issue. The entire change (stabilization?) in the body metabolism associated with puberty in the female, the cyclic change in the carbon dioxide combining power of the plasma (Bockelmann and Rother), the establishing of the calcium level (R. Rittman), and of the blood sugar level (Heilig and Hoff) are only a few of the known changes that occur.[45]

It is unnecessary here to review the various theories on the etiology of the epileptic convulsions. These may be found in the various systems of medicine and in monographs on the subject. Among the more recent studies of interest are those of Cuneo.[46] This investigator asserts that he has produced "epileptic convulsions" in animals following intravenous injection of the proteose substance found in the blood of epileptic patients following seizures. Cuneo found that the urine after epileptic convulsions showed a high percentage of organic acids, with a retention of the total nitrogen and an increase in the nitrogen content and continuous acidity of the feces. Patients fed high protein diets responded with a reduction of the acidosis and an improvement in the epilepsy. High carbohydrate diets produced an increase in acidity with a corresponding increase in the number and severity of the convulsions. Cuneo suggests a fault in the starch metabolism occurring in the first stage of conversion to disaccharides, maltose, lactose, cane sugar, etc. Normally this takes place through the action of amylolytic ferments, the subsequent conversion of maltose being effected by maltase ferment through hydration to glucose. The failure in the first stage resulted in the absence of sufficient amylolytic ferment, in the production of a more or less intense concentration of organic acids—acetic, butyric, lactic,

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42. Holt, L. E., Jr., La Mer, V. K., and Chown, H. B.: J. Biol. Chem. **64**:567 (July) 1925. Irving, L.: J. Biol. Chem. **68**:239 (May) 1926. Shohl, A. T., and Sato, A.: J. Biol. Chem. **58**:235 (Nov.) 1923; ibid. **58**:257 (Nov.) 1923. Shohl, A. T.: J. Biol. Chem. **50**:527 (Feb.) 1922; Physiol. Rev. **3**:509 (Oct.) 1923.

43. Greenwald, I., and Gross, J.: J. Biol. Chem. **66**:185-227 (Nov.) 1925.

44. Popea, A., and Vicol, A.: Compt. rend. Soc. de biol. **93**:749 (Aug.) 1925.

45. Hanse, A.: Zentralbl. f. Gynäk. **49**:529 (March 7) 1925.

46. Cuneo, Girolamo: Riv. Sper. di freniat. **45**:408 (Jan.) 1922.

tartaric, etc.—and these, which should normally have united with alkaline bases in the small intestine, pass in the epileptic into the blood and urine unchanged. The alkaline salts in the normal person are oxidized, through ammonium carbonate, into urea or, through sodium, into sodium carbonate. Cuneo concluded that this transformation of organic salts into sodium carbonate begins in the mucosa of the small intestine and is completed in the liver. The sodium carbonate is returned to the intestine in the bile. The lack of base favors the production of acidosis while a sufficiency of sodium tartrate favors the activity of the liver ferments and the production of sodium carbonate. "Epileptic convulsions" were produced in animals when sodium acetate and tartrate were injected intravenously. A proteose substance—nucleohistone—was consistently isolated from the carotid artery of the animals in the convulsions.

Osnato [47] in this country and Robertson [48] in England strongly support Cuneo's premises. It would seem, however, that the change in the acid base equilibrium of epileptic patients is toward the alkaline side preceding the attacks (as mentioned before). It can be demonstrated that a tendency toward alkalosis will precipitate convulsions [49] and an artificially produced acidosis will control the attacks.[50] Starvation is a most effective treatment in epilepsy,[51] and among other changes in the metabolism [52] starvation produces an acidosis.[53]

It is probable that certain epileptic patients do not develop an alkalosis preceding attacks; they may possibly develop an acidosis. A small number of patients with petit mal have developed grand mal convulsions on a high fat low carbohydrate diet.[50] The rôle of the blood sugar in convulsions has not been established.[54]

Robertson champions Cuneo's theory and adapts the old theory of

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47. Osnato, M.: Arch. Neurol. & Psychiat. **9**:488 (April) 1923.

48. Robertson, A. W.: Brit. M. J. **2**:119 (Dec.) 1924.

49. Peterman, M. G.: Ketogenic Diet in Epilepsy, J. A. M. A. **84**:1979 (June 27) 1925. Rosett, J.: Brain **47**:293 (Aug.) 1924. Georgi, F.: Klin. Wchnschr. **4**:2053 (Oct. 22) 1925.

50. Peterman (footnote 49, first reference) and article to be published.

51. Guelpa, G., and Marie, A.: Bull. gén. de thérap. **160**:616, 1910. Conklin, W. H.: J. Am. Osteopath. Ass., September, 1922. Geyelin, H. R.: Am. Soc. Clin. Invest., 1921.

52. Lennox, W. G.: Increase of Uric Acid in Blood During Prolonged Starvation, J. A. M. A. **82**:602 (Feb. 23) 1924; Arch. Neurol. & Psychiat. **11**:54 (Jan.) 1924; J. Biol. Chem. **66**:521 (Dec.) 1925.

53. Geyelin (footnote 51, third reference). Shaw, E. B., and Moriarity, M.: Am. J. Dis. Child. **28**:553 (Nov.) 1924. Gamble, J. L.; Ross, G. S., and Tisdall, F. F.: J. Biol. Chem. **57**:633 (Oct.) 1923.

54. Rumpf: Jahrb. f. Kinderh. **105**:37 (March) 1924. Wladyczko, S.: Presse méd. **33**:1475 (Nov.) 1925. Josephs, H.: Bull. Johns Hopkins Hosp. **37**:376 (Dec.) 1925; Fasting as Cause of Convulsions, Am. J. Dis. Child. **31**:169 (Feb.) 1926; Recurrent Vomiting, Am. J. Dis. Child. **31**:657 (May) 1926.

chronic intestinal stasis [55] to it.[48] Fortunately, Robertson's suggested "colectomy if it were not so dangerous" has been discarded.

The uric acid,[56] cholin,[57] carbamic acid [58] and urea-ammonia [59] theories have not been substantiated.

Pfeiffer and his associates [60] found epileptic patients to excrete large amounts of a ferment splitting glycyltryptophane after seizures. Before attacks, the substance was found in the blood and absent from the urine. After attacks the substance was found only in the urine. The colon was considered the possible origin of the glycyltryptophane. Chronic constipation is a common symptom in epilepsy as in other neuropathic diseases. The symptom does not cause convulsions.

Georgi,[61] using Rosett's [62] hyperpnea method to produce convulsions, studied the resulting changes in the blood colloids in epileptic patients. He studied especially the sedimentation, fragility, erythrocyte count, viscosity, refraction and coagulation time, and observed remarkable changes between the "proteinogenic changes of stability (pregnancy, fever, etc.) and the ionogenic (hyperpnea) changes." Georgi attributed the seizures to a combination of various factors, a disturbance of metabolism, ionogenic changes of stability of the colloids especially in the membranes, and a pathologic change in the cortex. New electrometric methods for the determination of the hydrogen ion concentration of the blood and plasma will be of great value in the further study of the genesis of epileptic seizures.

Rosett [62] has offered an excellent diagnostic aid in neurologic diagnosis which is of value in questionable cases of epilepsy:

> When a normal person breathes as deeply as he can without undue discomfort at the rate of twelve respirations a minute, manifestations of tetany become pronounced in from fifteen to thirty minutes. . . . The manifestations of tetany induced by the method in question in persons afflicted with defects of the central nervous system exhibit numerous deviations from the foregoing (normals). These affect the time of onset, the extent, and duration of the abnormal movements, the incidence of the rigidity in certain parts, the pattern formed by the segments of those parts, and the conscious state. On the whole, it is certain that different slight abnormalities of the central nervous system which are not, under ordinary conditions, manifested by definite signs and symptoms, are signaled during hyperpnea in a striking manner and in a number of ways.

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55. Bolten, G. C.: Rev. Neurol. & Psychiat. **12**:231, 1914.

56. Haig, G.: Brain **19**:68, 1896.

57. Donath: Deutsche Ztschr. f. Nervenh. **32**:232. Quoted in Block-Tice's Practice of Medicine, W. F. Prior Co., 1921, p. 409.

58. Krainsky: Allg. Ztschr. f. Psychiat. **54**:612, 1897.

59. Alexander, D. M.: Lancet, Oct. 14, 1911, p. 1072.

60. Pfeiffer, H.; Standenath, F., and Weeber, R.: Klin. Wchnschr. **4**:1122 (June) 1925.

61. Georgi, F.: Klin. Wchnschr. **4**:2053 (Oct.) 1925.

62. Rosett (footnote 49, second reference).

The hyperpnea produces a definite alkalosis,[62] which will precipitate latent convulsions.[63] Convulsions may also be precipitated with an alkalosis produced by the oral administration of soda bicarbonate in extremely large doses.[50] This procedure is not without danger.

Focher [64] describes a new diagnostic symptom in idiopathic epilepsy. With Spearman's esthesiometer he determines the tactile discrimination (Weber's tactile sensibility) between two sides. There is a marked difference between the two sides in 31.5 per cent of epileptic patients examined. This symptom, however, would indicate any cortical injury.

Stiefler [65] found C. Mayer's finger thumb reflex practically always absent during an epileptic seizure including petit mal of long duration. Mayer's reflex elicited by strong passive flexion of the basal phalanx of a finger (with the hand supinated) causes an opposition movement of the metacarpus of the thumb with flexion of the basal and extension of the second phalanx. This reflex is present in 96.5 per cent of normal persons. The reflex center is in the nuclei supplying the small muscles of the thumb.

Most cases of epilepsy react with a positive Babinski reflex (plantar extension) during a convulsion,[66] but there may be variations.[67]

Muck [68] found fifty-six of 100 epileptic patients to show the sign described for sympathicotonic migraine. When the mucous membrane of the nose is sprayed lightly with epinephrine and then irritated by touching with a sound, white lines appear which persist after the ischemia is gone. This sign is not constant.

Patterson's [69] hematologic picture for epilepsy (leukocytosis) cannot be confirmed.

The treatment of epilepsy remains a problem. Phenobarbital (luminal) (and its salts) is the most effective drug available.[70] It is justly supplanting the bromides.[71] Favorable results have been reported

63. Peterman (footnote 50, second reference). Georgi (footnote 61) Guillain, G.; Alajouanine, T., and Thévenard: Bull. et mém. Soc. méd. de hôp. de Paris **49**:341 (March) 1925. Stiefler, G.: München. med. Wchnschr. **72**:342 (Feb.) 1925.

64. Focher, L.: J. Nerv. & Ment. Dis. **62**:337 (Oct.) 1925.

65. Stiefler, G.: München. med. Wchnschr. **72**:342 (Feb.) 1925.

66. Shearer, C.: Lancet **208**:1341 (Jan.) 1925. Walshe, F. M. R.: Lancet **208**:65 (Jan.) 1925.

67. Tournay, A.: Arch. Neurol. & Psychiat. **13**:592 (May) 1925.

68. Muck, O.: München. med. Wchnschr. **72**:1543 (Sept.) 1925.

69. Patterson, H. A.: Am. J. Psychiat. **2**:427 (Jan.) 1923.

70. Grinker, J.: Phenolbarbital in Epilepsy, J. A. M. A. **79**:788 (Sept. 2) 1922.

71. Ashmore, B. L.: Boston M. & S. J. **187**:950 (Dec. 28) 1922. Wender, L., and Sampson, D. G.: New York M. J. **116**:336 (Sept.) 1922.

with the ketogenic or high fat diet.[72] These results await confirmation by others.

Craniotomy and the radical surgical measures have probably fallen into disuse. Such operations as ganglionectomy,[73] resection of the choroid plexus,[74] and pneumencephalon [75] cannot be recommended. The best treatment for epilepsy at present is a combination of proper dietetic measures, psychotherapy, and phenobarbital as indicated.

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72. Peterman (footnote 1). Krumholz (footnote 14, first reference). Peterman (footnote 24 and footnote 37, first reference); Minnesota Med. **7**:708 (Nov.) 1924; Am. J. Nursing **26**:267 (April) 1926; J. A. M. A., to be published; Med. Clin. N. Amer. **8**:1351 (Jan.) 1925.

73. Wagner, A.: Zentralbl. f. Chir. **52**:637 (March) 1925.

74. Polya, E.: Zentralbl. f. Chir. **52**:2404 (Oct.) 1925.

75. Trömner, E.: Klin. Wchnschr. **4**:1065 (May) 1925.

News and Comment

DEATHS ABROAD

Aguilar Gordon, distinguished Spanish pediatrician, director of milk distribution center for babies. He was the author of a book on Normal and Pathologic Physiology of the Child.

Minister Louis Comte, of France, promoter of children's institutes in the mountains, functioning for thirty years. Debilitated children of town workers are sent to the mountains, where they live in the homes of reliable farmers for six weeks in summer. The death of M. Comte causes unanimous regret.

INTERNATIONAL CONGRESS FOR PROTECTION OF CHILDREN

The Fifth International Congress for Protection of Children, which took place in Madrid, from April 4 to 8, 1926, decided that the Sixth Congress will be held in Paris, in 1928.

INSTITUTE FOR TREATMENT OF TUBERCULOSIS

Prof. Gregoris Araoz Alfaro, president of the National Department of Hygiene in Argentina, had crowned his scientific and humanitarian work by creating an Institute for the Study and Treatment of Tuberculosis. It will include laboratories for research work, a 150 bed hospital for children and adults; there will be courses on tuberculous diseases and veterinary medicine; a public lecture hall, a school for visiting nurses and a dispensary. Professor Alfara himself donated 100,000 pesos and Dr. Urquiza, 10,000 pesos. Owing to a large subscription, the organization will soon possess the necessary millions. The Institute will be erected in a populous district. It should serve as a model institution for other countries.

DANISH PHYSICIANS TO MEET

A meeting of Danish physicians and pedagogues will take place in the middle of August in Copenhagen. Inspectors of children's homes are invited. Similar meetings have already been held in Stockholm, Göteborg and Oslo. Physical training and games, school hygiene, feeding and utilization of leisure time will be among the questions treated. The program includes visits to various schools and institutions, excursions and an exhibition. The subscription fee is ten Danish crowns.

DEATH OF JOHN THOMSON, M.D.

The *Edinburgh Medical Journal* for August, 1926, announces the lamented fact of the death on Friday July 2, in Edinburgh, of Dr. John Thomson, a great pediatrician and beloved colleague. Dr. Thomson was 70 years old, and

succumbed after a short illness. The profession in America will greatly miss this teacher whom they so highly respected, and whose writings were of such great interest. During the past year, an effort was made by the Section on Diseases of Children of the American Medical Association to induce Dr. Thomson to come over as a guest. However, he never recovered his strength following an illness in September, 1925, although he continued working on the last edition of his book on the "Clinical Study and Treatment of Sick Children." His photograph and several pages devoted to his life will be found in the *Edinburgh Medical Journal.*

Abstracts from Current Literature

Pathology, Bacteriology and Biochemistry

THE ORGANISM OF ACTINOMYCES-LIKE TONSILLAR GRANULES. RUTH TUNNICLIFF, J. Infect. Dis. **38**:365 (April) 1926.

Tunnicliff succeeded in isolating from an actinomyces-like tonsillar granule a weakly gram-positive flexible motile anerobic organism, that produces in pure culture rosettes and test-tube brush-like forms, similar to those seen in the original material.

KENNEDY, Rochester, Minn.

PHYSIOLOGY OF BLOOD CLOTTING: THEORIES OF THROMBOSIS. A STUDY OF PRACTICAL METHODS FOR DETERMINATION OF CLOTTING TIME. T. L. RAMSEY, Ohio State M. J. **22**:117, 1926.

Ramsey, by description and graphically by chart, gives the physiology of blood clotting through four phases. A second chart illustrates the factors concerned in preventing coagulation. The third chart shows what actually occurs in normal blood physiology within the blood vessels. A fourth chart gives all factors, but with normal blood balance lost and the resulting clot formation. He discusses the characteristics of the clot, the various theories of thrombosis, the factors that have a bearing on the coagulation rate, and gives the modification of the Lee and White method for determining the rate, now being satisfactorily used in St. Vincent's Hospital Laboratory at Toledo, Ohio.

HORTON, Columbus, Ohio.

STUDY OF PARASITIC AMOEBAE BY EXPERIMENTAL CROSS INFECTION OF LABORATORY ANIMALS. S. F. CHIANG, Nat. M. J. China **11**:440, 1925.

This study was made (Harvard Medical School) "to determine whether the dysentery amoeba may be transmitted to the rat or to the mouse, and if this is possible, to see how long it will persist in these animals." During the course of the study, the author found that two or perhaps three species of amebae were found in normal laboratory rats, namely, *E. histolytica* (murina), *E. muris* and *Endolimax muris*. A method of raising ameba-free young rats was developed by laboratory breeding with the combination of high enema examinations. The author carried out two series of experiments of infecting rats with *E. histolytica* of human origin by mouth and per rectum, with positive results. "The identification of *E. histolytica* was done by morphologic study, cultivation and pathogenic tests in kittens. The author felt that his investigation yielded evidence that the rat is a carrier of *E. histolytica*, the causal agent of amebic dysentery." Numerous plates and a bibliography are appended.

THE VITALITY OF PLAGUE BACILLI IN STAINED SMEARS. H. M. JETTMAR. Nat. M. J. China **12**:1, 1926.

This author decided to imitate in every respect the ordinary method of smearing and staining plague bacilli on slides, using an inguinal bubo from a guinea-pig which had recently succumbed to plague. He describes his method, and gives charts showing number, etc., of guinea-pigs inoculated with the emulsion of smears from the inguinal bubo. With one exception (a guinea-pig

that died of pneumonia), typical plague bacilli in smears and cultures were obtained in every case. Intensive fixation by passing through the flame does not kill the bacilli in thin smears from a plague bubo, neither does short fixation by alcohol after passing through the flame do this with certainty, and preparations stained with diluted carbol fuchsin may still contain living plague bacilli even when treated with alcohol previously for a short time; even the wash from the stained plague smears may contain plague bacilli and must be disinfected, as well as the filter paper used for drying the stained preparations. Staining with concentrated alkaline methylene blue does not seem to kill bacilli. "As some of the infected animals succumbed and others did not fall sick at all, it has to be supposed that only a few plague bacilli were alive in the stained smears." Even the simple drying at room temperature was enough to protect one of the guinea-pigs, cutaneously inoculated, against infection.

TRANSMISSION OF TYPHOID FEVER BY BEDBUGS. LYNN-GE, Nat. M. J. China **12**:62, 1926.

As bedbugs are widely distributed throughout China, the author thought it would be interesting to find out whether they, like members of the louse family, transmit typhoid or not. He found typhoid bacilli on various parts of the bedbugs which had been on a sick rat for seven or eight days. He felt that his experiments showed conclusively that typhoid fever can be transmitted by these bugs. Numerous tables and a bibliography are appended.

LUCAS, San Francisco.

Nutrition

THE NUTRITIONAL REQUIREMENTS OF NURSING MOTHERS. THE EFFECT OF LOWERING BOTH THE ANTIRACHITIC VITAMIN AND CALCIUM IN THE DIET OF THE MOTHER UPON THE DEVELOPMENT OF RICKETS IN THE YOUNG. AGNES H. GRANT, Am. J. Hyg. **6**:228, 1926.

The effects of lowering both the antirachitic vitamin and calcium of the mother's diet are seen in the retarded growth of the young when they are kept on a uniform low calcium, low vitamin diet, as well as in the change in the type of rickets which develops on this diet, and in the increasing readiness with which the disease attacks the spine.

The rate of growth of the young, after weaning, is correlated with their weight when they are weaned, and on the length of the interval before they begin to develop signs of rickets. The weight curves flatten as the disease develops, until finally all growth ceases, and the weight curves become straight lines.

The age at which the young begin to develop signs of rickets, the rapidity with which the disease develops, and the severity of the final lesions depends more on the diet of the mothers than on the weight of the young when they are weaned; the largest and most resistant of the young from mothers on rachitic diets develop rickets at an earlier age, and in a more severe form, than the lightest weight young from mothers on a complete diet.

The type of rickets which develops in young that are kept on a uniform low calcium and vitamin diet changes from the slow progress of the chronic type of this disease to the rapid development of the acute types, as the vitamin and calcium content of the mothers' diets are progressively altered from the diets

which are rich in both calcium and vitamin to those which are deficient in both of these factors.

The increasing readiness with which rickets attacks the spine in the young that are kept on the uniform rickets producing diet is a fairly accurate index of the kind and amount of the calcium and vitamin deficiency in the mother's diet.

AUTHOR'S SUMMARY.

VARIATIONS IN THE FAT-SOLUBLE VITAMIN CONTENTS OF EGGS, RESULTING FROM DIFFERENT METHODS OF PRESERVATION. IRA A. MANVILLE, Am. J. Hyg. **6**: 238, 1926.

Three lots of fresh eggs were gathered from the same source at the same time of the year. One lot was placed in cold storage for one year; another was placed in water glass for eighteen months, and the third lot was used to establish standards by which the first two could be compared. The ether extract of the yolks was fed in amounts ranging from 0.25 per cent to 5 per cent.

By comparison of the resulting data it was determined that cold storage eggs lose not less than 75 per cent of their vitamin value; water glass eggs 50 per cent and frozen eggs something less than 50 per cent. It was found possible to maintain rats in a fairly normal condition by as low an amount of egg oil as 18 mg. a day. It is probable that this can be reduced still further.

By feeding graduated amounts of egg oil (fat-soluble vitamin), it was found that there is an optimal level at which this vitamin can be fed, and that apparently as much harm results from an excess as from a partial or complete lack of this principle. Spring eggs contain more vitamin than winter eggs, and it appears that hot-house vegetables (lettuce) have less value than vegetables which have been grown in the field.

AUTHOR'S SUMMARY.

DIFFICULTIES OF MATERNAL NURSING. HERMAN B. SHEFFIELD, M. J. & Record **123**:106 (Jan. 20) 1926.

The author believes there are three types of nursing mothers: one group that can nurse their babies, and who either nurse or do not nurse to suit their own convenience. To this group belong mainly the foreign born women of little or moderate financial means. Under all circumstances they are fully capable of nursing their offspring. In strong contrast to this group of primitive mothers, we meet the group that embraces the product of modern civilization. These mothers are anxious to nurse their babies, but in spite of the best surroundings are not capable of doing so. The third group of mothers are hindered from nursing their babies by a large number of traditional hard and fast rules being enforced on them, such as forced feeding and the preposterous rule of putting the infant to the breast at regular intervals. The view held by so many breast milk fanatics that the breast fed infant is less susceptible to infectious diseases than the bottle fed is at least a gross exaggeration of but a scintilla of the truth. Patients should be delivered at home when at all possible, as the idea of going to hospital has a depressive effect on them, and they and their babies are more exposed to infections which may directly or indirectly interfere with maternal nursing. The quality of the milk can be determined by laboratory tests and by the appearance of the stools. If the milk agrees with the baby, it will be satisfied after nursing peacefully for ten minutes. If the infant is not thriving satisfactorily on the breast milk, bottle feeding should be resorted to.

CORN MEAL IN INFANT FOOD MODIFICATIONS. GEORGE DOW SCOTT, M. J. & Record **123**:110 (Jan. 20) 1926.

In this article the author divides cereals in general into three groups:

(1) Oat group. The typical muscle or energy producing food; (2) the wheat group; (3) the maize group. The fat and heat producing food.

The composition and the nutritional contents of cereal grains are then discussed. Corn and corn products are of great nutritional value. McCollum has summarized some interesting tests. He showed that cattle fed on only a corn ration for a year were in an excellent state of nutrition, that they carried their young to full time. The young were vigorous and normal in size, and all lived and developed in a normal manner. Cattle fed on other cereals did not do so well. They were small of girth, they did not carry their young to full time, and the young died in a few hours or were born dead. Corn must be ground in a special way in order to give it its greatest food value, and for infants must be cooked for a long time, preferably by the process of steaming.

About the fourth or fifth month, one-half ounce should be given at first once a day, and a little later twice a day. The results from clinical experiments with the yellow corn meal leads the author to believe in the higher potency and higher energy value corn possesses over the other cereals.

WILLIAMSON, New Orleans.

DIET AND DISEASE, WITH SPECIAL REFERENCE TO THE TEETH, LUNGS AND PRENATAL FEEDING. EDWARD MELLANBY, Brit. M. J. **1**:515, 1926.

The author describes animal experiments showing the harmful effect of excessive oatmeal in the production of defective teeth. His further observations and comments concerning the "Catarrhal Child" are most illuminating. The catarrhal condition in children may develop at any time but often in the first few weeks of life before postnatal conditions could possibly be responsible for the apparent absence of resistance to infection. The author considers that such lowered resistance can be explained by defective feeding of the mother during pregnancy, and the defects are probably of the type indicated by some of the experimental work on animals described in his lecture — namely, a deficiency in the diet of foods containing fat soluble vitamin, such as milk, eggs, butter, cheese, animal and fish fat, and a relative excess of cereals such as bread, oatmeal and rice, and other foodstuffs deficient in vitamin A.

Not only is there some experimental support for the suggestion, but experience shows that the dietetic defects described are those most commonly met with in human feeding. It is, therefore, probable that these defects of diet of women during pregnancy and lactation are responsible for some, and possibly much of the illness and mortality of young infants. His conclusions are:

1. It has been shown experimentally that these defects in the maternal diet increase the tendency of the offspring to develop rickets.

2. The same defects in the diet seem, on the basis of statistics, to increase the susceptibility of young animals to bronchopneumonia and inflammatory conditions of the respiratory tract, and, in general, to result in puppies of lowered vitality.

3. It is well known that the catarrhal child may develop this condition shortly after birth, and that it has a great tendency to become rachitic and to develop bronchopneumonia.

4. Puppies which develop rickets when feeding on these experimental diets frequently develop a catarrhal condition of the alimentary tract sooner or later, the time seeming to depend partly on the kind of feeding of the mother and the puppy in the preexperimental days.

THE VALUE OF IRRADIATED CHOLESTEROL IN THE TREATMENT OF RICKETS. LEONARD PARSONS, Brit. M. J. **1**:519, 1926.

The author cites a case of rickets which had been previously treated with cod liver oil for the greater part of a year with little or no improvement. Irradiated cholesterol was administered, with the result that the rickets was promptly cured. The inorganic phosphorus before treatment was 4.67 mg., and at the conclusion of the three months therapy with active cholesterol was 6.8 mg. The blood calcium also rose from 7.15 to 10.4 mg. Roentgen-ray evidence confirmed the cure. Unfortunately, the author did not state the dose of the cod liver oil previously given, and whether or not it was active; however, the case report very definitely shows the curative properties of freshly irradiated cholesterol. Overirradiation of this substance renders it inactive.

BROWN, Toronto.

THE SIGNIFICANCE OF COWS' MILK WHEY FOR THE GENESIS OF ACUTE DIARRHEAL DISTURBANCES IN BABIES. FIFTH COMMUNICATION — COWS' WHEY AND BLOOD SUGAR. KLAUS KEILMANN, Ztschr. f. Kinderh. **40**:259, 1926.

The next approach is by the determination of the effect of albumin, salts and sugar on the blood sugar curve of infants. There was a definite delay in the hyperglycemia in the case of whey as a whole, which must have been due to a transient damage done by it to the absorption power of the intestinal mucous membrane. Albumin, by itself, is without effect, and so is casein. The salts and sugar caused a normal rise in the blood sugar curve but a slow and irregular return to normal. Because this result disappeared with the separation of the salts by dialysis from the albumin-free whey, it must be that the salts hindered the absorption or slightly disturbed the intermediate sugar metabolism.

THE SIGNIFICANCE OF COWS' MILK WHEY FOR THE GENESIS OF ACUTE DIARRHEAL DISTURBANCES IN BABIES. SIXTH COMMUNICATION — SUGAR ABSORPTION IN HUMAN MILK, COWS' MILK, UNDILUTED AND DILUTED, AND EIWEISSMILCH. KLAUS KEILMANN and FLORA ROSENBUND, Ztschr. f. Kinderh. **40**:268, 1926.

The third approach is by the determination of the effect on blood sugar curves by different kinds of milk. There was a normal curve with human milk, but whole cows' milk caused the same delay in the absorption of sugar as whey did. By dilution of the milk, one to two, with water, this delay disappeared. Albumin milk has a whey content of 50 per cent, and its effect was to cause a faster absorption than whole whey and a slower one than with human breast milk or milk sugar solution. By the similarity of the blood sugar curves of human milk and milk sugar solution, it is obvious that quick absorption does not depend on a stimulating effect on the intestinal mucosa by natural as compared to foreign milk. The delayed absorption of sugar in the case of cows' milk is to be referred to the injury done to the intestines by the foreign whey.

EMERSON, Boston.

CONGENITAL ECCHONDROSIS. F. SPEISER, Virchows Arch. f. path. Anat. **258**:126, 1925.

Speiser describes a case of generalized ecchondrosis in a boy who died at the age of 4½ years. The periosteum, the growth cartilages of the epiphyses of the long bones, the cartilage between the osteogenic centers of the bones and the cartilages of the synchondroses all took part in the proliferative process. The latter is considered a developmental anomaly which has its origin in the fourth to either fetal month.

O. T. SCHULTZ.

Prenatal Conditions

REPORT OF A CASE OF ECTOPIA VISCERUM, RACHISCHISIS, MALFORMATION OF THE SACRUM, PELVIS INVERSA, HYPOPLASIA OF THE THORACIC DUCT, AGENESIS OR HYPOPLASIA OF VARIOUS ABDOMINAL VISCERA AND PLACENTA PREVIA. RALPH G. MILLS and BERNARD E. WALPERT, Am. J. Obst. & Gynec. **10**:10, 1926.

The combination of fetal defects may vary in almost innumerable ways. Authors in the past have postulated theories in like number to account for the developmental defects they observed. Mills and Walpert have reviewed the literature in major cases similar to theirs. They call attention again to the possible influence of fluid accumulations in the body, and the results of changes in osmotic pressure at different stages of development, to account for at least the major part of the defects present in their case.

CONGENITAL HERNIA AT THE LINEA ALBA. H. R. CHARLTON, Am. J. Obst. & Gynec. **10**:103, 1926.

The author was able to collect 250 case reports of congenital hernia of the linea alba up to 1925, and adds another case report with the technic of repair.

Operation can be carried out with very little or no anesthesia, but chloroform should be used if necessary.

The overlying sac of amnion and Wharton's jelly is peeled off and the mass reduced. Occasionally it is necessary to remove part of the liver to restore the mass to the abdomen. The mortality is approximately 30 per cent.

ALLEN, Chicago.

CONGENITAL MALFORMATIONS OF THE RECTUM AND ANUS. J. F. SAPHIR, M. J. & Record **123**:109 (Jan. 20) 1926.

Because of the rarity of the condition the author reported the following three cases:

Case 1.—B. H., a boy, aged 14 months, apparently healthy, who on rectal inspection showed the presence of a fold of skin obstructing the anal opening and extending anteriorly to the scrotum. Underneath the fold there were tracts filled with fecal particles. These simulated fistulous canals. The fold of skin was excised under procaine anesthesia, and a congenital marrowing of anus and rectum were split posteriorly. Dilatation of anus and rectum were carried out for about eight weeks.

Case 2.—A girl, aged 5 weeks, revealed a distant occlusion of the anus by a transverse fold of skin which projected backward to the tip of the coccyx.

Case 3.—A girl, aged 4½ months, on examination revealed a pin point opening where the anus should have been. The child had never passed by the bowel anything more than discolored fluid, and on arriving at the office was crying, with the abdomen distended, legs flexed and severely straining.

Both these patients were operated on by the author under procaine anesthesia with immediate relief.

WILLIAMSON, New Orleans.

Diseases of the New-Born

NOTES ON THE ETIOLOGY AND EPIDEMIOLOGY OF IMPETIGO CONTAGIOSA NEONATORUM. DAVID L. BELDING, Am. J. Obst. & Gynec. **10**:70, 1926.

In three epidemics of impetigo contagiosa neonatorum occurring in the Robinson Memorial Hospital of Boston, an attempt was made to trace the etiologic and epidemiologic factors. As usual, each succeeding epidemic seemed to show a gradually decreasing virulence of the infecting organism. The mortality varied from 25 per cent in the first epidemic to no deaths in the last. Most of the cases recorded occurred between the fourth and the seventh days.

The prevailing organism was *Staphylococcus aureus,* although *Staphylococcus albus,* a gram-positive bacillus and *Streptococcus hemolyticus* were occasionally found. There seemed to be different strains of *Staphylococcus aureus* and the pathogenic action also varied. Variations occurred also with different strains in the different epidemics.

Inoculation of the infant with cultures obtained from other vesicles seemed to show more typical bleb formation with *Staphylococcus aureus* than with *Streptococcus hemolyticus.* Inoculation of an adult with the same culture gave an acutely inflamed area but no bleb formation.

Transmission seemed to occur both from human contact and inanimate objects. The institution of prompt isolation is the only means to limit the spreading infection to other infants.

ALLEN, Chicago.

PRODUCTION OF CEREBRAL AND VISCERAL HEMORRHAGES IN THE YOUNG RAT; AN EXPERIMENTAL STUDY; PRELIMINARY REPORT. IRA A. MANVILLE, JESSIE LAIRD BRODIE and C. ULYSSES MOORE, Northwest Med. **25**:205 (April) 1926.

The authors fed albino rats on a diet adequate for growth, nutrition and reproduction, but inadequate for satisfactory lactation. On this diet, the young dying before weaning almost invariably show intracranial and visceral hemorrhages. These hemorrhages were either fulminating or insidious in type. In their earliest stages these are punctate, later becoming confluent.

SCOTT, Philadelphia.

A CONTRIBUTION TO THE STUDY OF BLOOD DISEASES IN THE NEW-BORN. EUGENE STRANSKY, Rev. franç. de Pédiat. **2**:26, 1926.

Whatever may be the source of blood diseases in infants, there is no evidence that they are transmitted from the mother to the new-born. Several cases of leukemia, one of pernicious anemia and one of septicemia in pregnant women are cited in which the infants showed no signs of disease. Anemias in the infant may be congenital or brought about by a known or unknown cause in the first few days of life. In the former group, the case of Susstrunk is cited; the child was born with an hemoglobin of 26 per cent and died on the

second day, the liver and spleen showing deposits of hemosiderin and also blood forming centers. Other cases of anemia with enlarged liver and spleen fall into the group of congenital syphilis, and it is felt that many cases designated by the older authors as congenital leukemias and congenital edemas were really syphilitic in origin.

Cases which may be considered as lymphatic leukemia have been on record since 1888, but it was not until 1924 that myeloid leukemia was described in the new-born. The author was the first to recognize a case of this kind during life. From birth, the baby presented slightly elevated livid spots disseminated over the skin surface. On admission to the hospital at the age of 3 weeks, petechiae were present over the skin of the abdomen and buccal mucous membrane. The liver, spleen, and lymph nodes were greatly enlarged. The white count was 181,000, with 86 per cent myeloblasts (identified by the oxidase reaction). Death occurred on the fifth day. Histologic examination showed myeloid metaplasia of the spleen and lymph nodes, and extensive myeloid infiltration elsewhere. A case with similar findings, but with a chronic course was described by Malmberg (Stockholm).

LESLIE, Chicago.

INTRACARDIAC INJECTION OF EPINEPHRINE FOR THE RESUSCITATION OF NEW-BORN INFANTS. S. VON WACHENFELDT, Monatschr. f. Geburtsh. u. Gynäk. **72**:185 (Feb.) 1926.

A review of the literature on intracardiac injection of epinephrine is presented. Von der Velden introduced the measure clinically in 1906 after Winter had used it in rabbits. Von Wachenfeldt revived two apparently stillborn infants with 1 cc. and 0.5 cc. of epinephrine. He advises, however, a dose of 0.06 mg.

PETERMAN, Milwaukee.

Acute Infections

LAMBLIASIS ENTERITIS. R. MILLER, Arch. Dis. Child. **1**:93 (April) 1926.

Lamblia infections have become common in England only since the war. Miller reports twenty-three cases, the patients ranging in age from 3 months to 14 years. The "majority" of patients were said to have a "chronic diarrhea." Insufficient evidence is presented to substantiate the conclusions that lamblia is the etiologic agent in the cases presented.

PETERMAN, Milwaukee.

CEREBROSPINAL MENINGITIS. C. H. HOFRICHTER and JOHN W. UNIS, Northwest Med. **25**:245 (May) 1926.

Hofrichter and Unis report eleven cases treated by them in the Seattle City Hospital. The cases were found in locations where people were closely grouped together. Two came from one lodging house and three from another. All of these patients were adult males. The early symptoms of meningitis are indistinguishable from those of influenza, and only when signs of cerebral irritation occur is the diagnosis clear. The writers consider cervical rigidity and Kernig's sign the most important diagnostic signs. Two of the patients showed purpuric spots. The writers administered serum frequently and continued it for some time after the disappearance of the clinical signs. Four of the eleven patients died. Six made a perfect recovery and one recovered, but was left with sequelae.

SCOTT, Philadelphia.

VARICELLA-MYELITIS. KNUD H. KRABBE, Brain **48**:535, 1926.

Acute myelitis may be caused by different acute infectious diseases, though cases following chickenpox are very rare. The author gives the history of his patient, a boy, aged 8 years, who was admitted to the hospital Feb. 25, 1925, two weeks after eruption of chickenpox. Ten days after the eruption he began to develop paralytic symptoms and five days later entered hospital. Five days after admission, the symptoms began to clear up. One month after admission, analgesia was completely gone and only a slight degree of tactile hypesthesia remained. He was discharged from the hospital April 13, completely cured, gait natural, disturbances of sensation entirely gone and tendon-jerks and the plantar reflexes normal. He was treated with methenamine for the first twelve days, and eight days after admission passive movements of the ankle were instituted to prevent equinus contracture; fourteen days later a night bandage was prescribed and one month after admission massage of the lower limbs was started. The author believes that this case of myelitis was due to varicella virus itself, and very improbably a secondary infection. "The favorable course of the disease agrees with the good prognosis of chickenpox." He reviews the few cases of varicella-myelitis that have been reported, and cites some rare cases of encephalitis, hemiplegia, etc., associated with chickenpox. A bibliography is appended.

LUCAS, San Francisco.

AN EPIDEMIC ERUPTIVE DISEASE AMONG CHILDREN AT BUCHAREST. STROE, Arch. de méd. d. enf. **5**:255 (May) 1926.

During the winter of 1923, Stroe had occasion to observe, in a crèche at Bucharest, an epidemic which, from the point of view of symptomatology and mode of transmission, distinguished itself from all known infections of infancy. After a period of five months, during which about two thirds of the infants were stricken, the disease spread throughout the neighborhood, especially among school children, where it was diagnosed by some as scarlet fever and by others as measles.

Definition: An epidemic, eruptive, contagious and infectious disease characterized by a period of invasion, during which the mucus from the nose, mouth and pharynx is streaked with blood, followed by a scarlatinal or morbilliform eruption accompanied by vesicles. This eruption is succeeded by desquamation.

Epidemiology: The first case appeared Jan. 11, 1923, in an infant confined in Room 2, Pavilion A, of the Crèche "Ecaterina." This pavilion was comprised of 4 rooms of 14 beds each. As soon as the case was discovered, it was isolated, and the usual precautions were taken for scarlatina. The following day another child, in the same room, was taken sick and likewise isolated. Both patients recovered promptly and were returned to their room. On February 15, the first infant mentioned had a relapse and was again placed in quarantine. March 5, the second infant had a return of the disease and infected a third child, cared for by the same wet nurse, this baby being seized on March 20. Two other infants in this room became ill on March 25 and 26, respectively, or twenty and twenty-one days from the relapse of infant number two. Such was the début of the epidemic in this ward; twelve days later identical cases appeared in the neighboring wards of Pavilion A.

In Pavilion B, the first case was found on January 24, and was isolated until February 18. On that date, the second case appeared, and from then on there developed one or two new cases daily, seventeen infants being ill at one time, and only four of the forty-two infants in the pavilion escaping infection. All of those remaining free were under 2 months of age.

By the end of June, 1923, the epidemic had entirely subsided in the crèche, but during the summer and autumn following, scattered cases began to appear throughout the city, identical in every respect with those described in the foregoing. Occasionally, one would find all the children of a certain family stricken, and, in the winter of 1923-1924, older children were affected, so that in some schools two thirds of the pupils were attacked. Stroe has seen no cases, however, in persons more than 10 years of age.

Etiology: The origin of the disease has, as yet, not been determined. Blood cultures and examinations of the mucus have been negative. Winter and early spring seem to be the favorite season for its propagation, and the crowding incident to hospital and school life favors it. It is probably conveyed not only directly but through the medium of nurses and attendants. Insects have been suspected, of course, but the most careful study has failed to incriminate them. Sex plays no rôle, but age is important, no case being found in those under 2 months or over 10 years.

Incubation: The average period has been from ten to fifteen days, but in a few cases it was found to be as low as six days.

Symptomatology: One may consider three separate phases under this head: 1. Invasion. This period lasts from two to five days and, though often unperceived, is characterized by sweating, oculonasal catarrh, fever and loss of appetite.

2. The Exanthem. This is the most constant and particular symptom of the disease. It is, in the majority of cases, scarlatiniform; occasionally it is similar to measles. The color of this rash varies from rose red to purple. At the time of its appearance, or on the following day, the vesicles appear. In rare cases the vesicles may precede the exanthem. These vary in size from the point of a needle to a millet seed, and frequently may only be perceived by stroking the skin with the hand. The fluid content is clear except in areas in which perspiration is profuse, when it becomes opalescent or of a citron hue. The eruption is frequently accompanied by itching, and may then be complicated with the lesions brought on by scratching. The duration of the rash is from three to seven days.

3. Desquamation. This exists in practically all cases, and its intensity depends on the depth of the exanthem and the number of vesicles. It is of a furfuraceous character but more abundant than in measles. The desquamation never involves the palms of the hands or the soles of the feet.

Fever: Coming on without a rigor, the fever appears during the stage of invasion and continues throughout the period of exanthem, oscillating between 38 and 39 C., defervescence occurring always by lysis. In a few cases there are marked deviations from this rule.

Progress, Duration and Termination: From the foregoing it will be seen that we are dealing with an acute disease of multiple varieties, evolving in several stages, which may be protracted up to several weeks. In the epidemic studied at the crèche, there were six fatalities, due either to frank exhaustion or to pulmonary complications. Relapses were very common in this series.

Complications: These were confined for the most part to the respiratory tract, rhinitis and pharyngitis being pathognomonic signs of the period of invasion. Laryngitis was occasionally observed; tracheobronchitis more frequently and bronchopneumonia fairly often. Diarrhea was frequently noted at the beginning of the disease, but usually subsided. There were evidences in certain cases of greatly increased intracranial pressure which was promptly relieved by lumbar puncture; this was repeated every other day, in grave cases,

as an anticipatory precaution. Convulsions appeared in a few infants. A polydermatitis due usually to the staphylococcus was a complication frequently noted by Stroe.

Differential Diagnosis: The disease in question may readily be confused with scarlet fever, measles, the so-called "sweating disease" and with miliaria rubra.

From scarlatina it may be distinguished by:

1. The profuse perspiration, commencing with the invasion. 2. The miliary eruption. 3. The character of the desquamation which is never in flakes and never affects the palms of the hands or plantar surfaces of the feet. 4. The frequency of the relapses. 5. The scarlatinal polynucleosis is here replaced by a mononucleosis. 6. The oculonasal catarrh and the absence of sore throat and strawberry tongue.

From measles it may be differentiated by:

1. The absence of Koplik's spots. 2. The vesicular eruption. 3. Relapse and recurrence.

With the "sweating disease," however, it is not so easily differentiated, but we may note that in this disorder the incubation is shorter, the face often escapes the exanthem, the desquamation is in the form of scales and affects the palms and plantar surfaces. It attacks adults and is very rare indeed in nurslings; it spread only in the summer months and in rural districts, and is not characterized by relapses and recurrences. Vesiculation is rare.

Miliaris rubra is not an epidemic disease; it has no remissions, it does not affect the face, it continues but four or five days and has no exanthem.

Prognosis: The disease is, in general, benign; there were six deaths in forty-seven cases of our first series and no deaths in the second epidemic.

Prophylaxis: This consists in the prompt isolation of the sick infants.

Treatment: Antiseptic solutions were employed in the upper respiratory tract; antipyretics were used in small doses. In cases showing marked somnolence, lumbar punctures were recommended.

AMESSE, Denver.

A NEW ANTISCARLATINAL SERUM. S. P. CHEN, Nat. M. J. China **11**:219, 1925.

There is a great variety in the severity of scarlet fever in Pekin and in northern China; the cases are largely of "toxic" type with high mortality. During 1922-1923, the author took throat swabs from all severely ill subjects encountered in the Government Isolation Hospital, and had the laboratory isolate *Streptococcus hemolyticus* from each case, from which a serum was prepared which contained 19 strains of this organism. The advantage of this serum is that it is made of organisms isolated from really virulent cases, which are not seen elsewhere. He experimented with different amounts of this vaccine, giving it only to the severely ill subjects. The majority were given 25 cc., but larger initial dose and repetition of first dose depended on the clinical aspect of case, some requiring 50 cc. as initial dose, but 100 cc. in two to four injections was the maximum quantity required. When given early in virulent cases, it apparently prevented serious complications. It appeared "to benefit erysipelas developing in scarlatinal cases by cutting short the cause of the disease."

A PRELIMINARY NOTE ON THE PRODUCTION OF ANTISCARLATINAL SERUM. EDGAR T. H. TSEN and P. Z. KING, Nat. M. J. China **11**:224, 1925.

These authors describe the preparation of the serum used on Chen's patients, which is very different from that made by Dochez and by Dick. The authors' antigen consisted of "washed whole bacterial bodies — first dead and then

living." Briefly, the nineteen strains of hemolytic streptococcus isolated from the throats of scarlet fever patients were grown in 0.5 per cent glucose broth. After twenty-four hours' incubation at 37 C., the broth cultures were mixed together and centrifugalized. The supernatant clear fluid was then removed and the sedimented bacteria was suspended in physiologic sodium chloride solution. The new suspension is recentrifugalized and the sedimented bacteria is suspended in physiologic sodium chloride solution, strained, the bacterial count adjusted to 5,000 million per cubic centimeter and injected into a horse, dead cultures being used first. Altogether, twelve doses of dead and fourteen of living cultures in gradually increasing amounts were injected intravenously. Test bleedings were begun after the fifth injection of living culture. When serum was satisfactory by means of protection tests on mice, regular bleedings were made. The serum was separated from blood clot and preserved with 0.25 per cent tricresol and then tested for sterility, toxicity and potency. Further studies are being made.

THE SCARLET FEVER PROBLEM IN THE FAR EAST. LIN CHIA SWEE and H. M. JETTMAR, Nat. M. J. China **11**:399, 1925.

Scarlet fever is generally more severe in northern China than in corresponding parts of Europe and America. It compares with the mortality of foreign countries of the same latitude as northern China, showing a higher percentage in the latter. Out of 1,275 Dick tests made on Chinese in Harbin in ages from 1 to over 30 years, 47.7 per cent positive reactions were obtained. The authors also conducted Dick tests among 542 school children of six schools, and found 86 per cent positive in kindergartens. They had encouraging results from Dochez's serum made in America, but are preparing their own serum to try on a more extensive scale.

LUCAS, San Francisco.

Chronic Infections

FURTHER CONTRIBUTION TO THE PROBLEM OF CONJUGAL SYPHILIS OF THE NERVOUS SYSTEM. ALFRED GORDON, Am. J. Syph. **10**:1 (April) 1926.

In the study of conjugal neurosyphilis, one is first impressed with the probability that we are dealing with a special neurotropic strain of organisms. The following facts support this view: The spirochete isolated from paretic patients differs biologically from that found in chancres and mucous patches. Their effects on experimental animals differ as to incubation period, type and duration of the local lesions. Animals having an active immunity to the neurotropic strain were susceptible to the dermatropic infection, and vice versa.

The children of neurosyphilitic subjects are similarly affected, which may be a combination of hereditary predisposition and neurotropic organisms.

Then there is the "Exhaustion View of Edinger," of interest in connection with the cases showing a similarity of occupation. He cites one couple, both authors, who developed paresis, and another couple who were subjected to physical exhaustion who developed tabes.

In considering the etiology of conjugal neurosyphilis, the following factors must be borne in mind:

1. A special neurotropic virus. 2. Special predisposition. 3. Overfatigue of central nervous system. 4. Conjugal neurosyphilis may be represented by any of the various types of involvement, that is, paresis, tabes, vascular or meningeal syphilis.

A Study of Testes from Syphilitic Patients: Histologic and Inoculation Experiments. Eli R. Saleeby, Am. J. Syph. **10**:215 (April) 1926.

Saleeby found, microscopically, syphilitic changes in 57.5 per cent of testes in forty syphilitic patients. He was able to demonstrate the spirochete in only one, a 7 month fetus.

McBride, Iowa City.

Gold Compounds in Treatment of Experimental Tuberculosis of Skin in Animals. Jay Frank Schamberg, Malcolm M. Harkins and Herman Brown, Arch. Dermat. & Syph. **13**:43 (Jan.) 1926.

The literature concerning the use of gold and its compounds in the treatment of tuberculosis is reviewed, and the authors' experiments with various gold compounds are recorded. They conclude that, with the preparations used, a favorable though not a curative influence was induced. Their results lend encouragement to the hope that a gold compound may be found which will have a marked effect on tuberculosis.

So-Called Herxheimer Reactions. Karl Herxheimer and Hans Martin, Arch. Dermat. & Syph. **13**:115 (Jan.) 1926.

The Herxheimer reaction manifests itself in exacerbating syphilitic lesions associated with inflammatory changes following antisyphilitic treatment. The severity of the reaction and speed of appearance vary proportionately with the spirocheticidal activity of the drug employed, while the duration of the reaction varies inversely with such activity. The reaction following arsphenamine administration is likely to appear within two hours; more certainly within twelve hours. The reaction following mercury or bismuth administration often appears within twenty-four hours. For specific provocative diagnosis of skin lesions, the intramuscular injection of 1 cc. of a 10 per cent oily suspension of mercuric salicylate or, better, 0.15 to 0.2 Gm. silver arsphenamine is recommended. The explanation of the reaction is similar to that of the tuberculin reaction in which there is an intermediate reaction between the specific organism and the hypersensitive cells. In the sensitized tissue, through allergic and immune processes, a potential hypersensitiveness develops against the organisms. The potential hypersensitiveness is activated after the administration of specific drugs through their effect on the spirochetes with the development of hyperemia and edema.

Jeans, Iowa City.

Hookworm Disease in China. A Preliminary Report. W. W. Cort, J. B. Grant and N. R. Stoll, Nat. M. J. China **11**:282, 1925.

China hookworm commission undertook this investigation in June, 1923, with a threefold program of work: (1) To gain from all available sources information on the distribution and importance of hookworm disease in China; (2) to try by epidemiologic studies carried out under a series of typical conditions to analyze the factors influencing its spread, and (3) to study experimentally the relation of the use of human feces in fertilizing the crops to its etiology. They sent out questionnaires all over China, and over 150 answers were received from every part of China. The authors analyze the factors influencing the spread of hookworm disease in China — climatic, human fertilization in agriculture and relation of mulberry cultivation to infestation. They discuss the methods of control, which theoretically may appear simple but

which practically are complicated by the conservatism and poverty of the farmers, ignorance, and inaccessibility of districts to which transportation is difficult. They believe that the only hope lies in an adequate medical personnel among the Chinese themselves.

LUCAS, San Francisco.

Internal Diseases

NEPHRITIS AND ITS PROGNOSIS. D. PATERSON and W. G. WYLIE, Arch. Dis. Child. **1**:103 (April) 1926.

Acute nephritis is classified as (*a*) parenchymatous or "exudative" (tubulo-glomerulo nephritis, as postscarlatinal) and, (*b*) hemorrhagic (as associated with an acute pharyngitis). Twenty-two cases of parenchymatous nephritis resulted in four deaths and five complete recoveries, while in twenty-seven cases of hemorrhagic nephritis there were no deaths and ten complete recoveries.

PETERMAN, Milwaukee.

THERAPEUTIC PNEUMOTHORAX IN PULMONARY TUBERCULOUS CHILDREN. P. F. ARMAND-DELILLE, M. J. & Record **123**:113 (Jan. 20) 1926.

After trying various treatments for pulmonary tuberculosis, the author believes that artificial pneumothorax is the most favorable. In his article he gives the technic very briefly. No other curative method causes the disappearance of tubercle bacilli in a few weeks, with a real improvement in the general health. In certain cases the therapeutic pneumothorax is the only means of producing a complete cure; all the symptoms subsiding, with normal breathing, no bacilli, and normal roentgen-ray findings.

WILLIAMSON, New Orleans.

ENLARGED THYMUS WITH STRIDOR AND TETANY. LEOPOLD MANDEL, Proc. Roy. Soc. Med., Section for the Study of Disease in Children **19**:17 (Dec.) 1925.

The author reported a case of enlarged thymus, with stridor and tetany, in a breast fed infant aged 10 weeks. At first, the mother noticed the breathing was harsh, but after fourteen days it became croaky. Shortly after this, from time to time the infant would have slight fits in which the breathing would become noisy. There was distinct stridor and the infant would turn blue during an attack.

WILLIAMSON, New Orleans.

PYELITIS IN INFANCY AND CHILDHOOD. E. GORTER, Rev. franç. de Pédiat. **2**:1, 1926.

Among the variable symptoms of pyelitis in infancy, the two most constant are: (1) a rise in temperature which is not easily explained by physical signs in an infant formerly in good health, and (2) a marked pallor with slight puffiness of the face. The diagnosis is confirmed by examination of the urine. Under 1 year of age boys are affected almost as frequently as girls. The prognosis is good; when death occurs, the pyelitis is not the only, nor yet the principal cause of the fatal outcome. Few cases become chronic, and in such cases there is usually some congenital malformation of the urinary tract. However, children who have had a pyelitis frequently show a recurrence of symptoms with any acute disease.

The urine, if examined in the first few days of the disease, shows albumin, casts and often chromocytes, indicating that there is at this time some injury

to the renal parenchyma. This, together with the absence of a cystitis, in most of the severe forms found in infancy points to a blood stream infection rather than to an ascending one. The organisms most frequently found are varying types of colon bacilli, designated as para colon bacilli.

In treatment, the author strongly recommends the use of autovaccines, but the dosage and interval should be carefully adapted to each case. Some work was done using a bacteriophage but the lytic principle seemed to have no direct beneficial effects.

LESLIE, Chicago.

CONCERNING HERNIA PULMONALIS. M. BRUIN, JR., Jahrb. f. Kinderh. **108**:5-6, 1926.

A case of hernia of the lungs is reported in full; the main features may be recounted as follows: A girl, born at full term, the seventh child of healthy parents, was slightly cyanotic immediately after birth, but this condition did not persist. Breast feeding was discontinued after a few weeks, and the infant had not done well on artificial food. She was brought to the clinic on account of a nutritional disturbance. There had been some cough off and on for three months. On examination, a small body with relatively small head and a rather wedge-shaped forehead was seen; nothing unusual was noted further, except that on each side of neck, symmetrically placed anterior to the sternocleidomastoid muscles, there was a pea-sized wartlike elevation which did not seem attached to the underlying tissues and might be taken for a puckering of the skin. There was a moderate sized umbilical hernia and an indirect inguinal hernia on each side. On account of a systolic heart murmur and increased area of heart dulness on the left, and signs of diffuse bronchitis, a roentgenogram was made, with the following findings: On each side of the neck there was a light area with markings similar to those of normal lung tissue; the conclusion was that the lung apexes were forced up through the upper chest aperture and a true hernia of the lungs into the lateral triangles of the neck produced. With this in mind, more careful examination of the infant showed, on deep expiration, a ballooning out on both sides of the neck above the clavicles: this was entirely different from the increased thickness of the neck seen in normal children when they cry; it was large, more sharply localized and had the form of a blunt dome with its base disappearing below the clavicles and its top toward the cranium. From these findings and from repeated roentgen-ray observations, it seemed certain that this ectopic lung area was not directly connected with the larynx nor with the trachea. In a study of the several films made, it was noticed that the shape of this lighter area was not always the same; sometimes round as a ball and at other times elliptical.

Hernia of the lungs, strictly speaking, should not include those following perforating wounds of the chest, nor those due to sudden excessive intrathoracic pressure, as in whooping cough. When these are excluded, true hernia of the lungs seems to be of very infrequent occurrence. Defects due to anomalies in the development of the chest wall give opportunity for development of a lung hernia which is usually spoken of as congenital. The author has been able to find in the literature only two reports of cases resembling his own, namely, one reported by Hochsinger and the other by Mocera. In the cases described by these authors, the patients showed inflated lung tissue in the neck on both sides symmetrically situated, as in the case here described; in their patients also there were hernias in other parts of the body, showing probably an underlying general inferiority of fibro-elastic tissue.

A detailed discussion of the probable physiologic and anatomic reasons why the hernia increases in size during expiration is indulged in.

The author's differential diagnosis is very comprehensive and instructive.

PARMELEE, Chicago.

VACCINE THERAPY OF THE BACTERIAL DISEASES OF THE URINARY TRACT. JOSEF REJSEK, Cas. lek. Cesk. **64**:380 (March) 1925.

In the author's series of thirty-two cases, as in the many series cited, *B. coli* is the invading organism most often isolated. The author found *B. coli* in twenty-two cases, staphylococcus in seven, a diplococcus in two and pyocyaneus in one case. Of these thirty-two cases thirteen remained unimproved after autogenous vaccine treatment, and these were associated with some retention signs such as dilated calices, hydronephrosis or atonia of the bladder. The treatment is of greatest benefit in simple pyelocystitis.

STULIK, Chicago.

MOLD CASTS IN THE URINE IN A CASE OF DYSURIA. E. GUNDERSEN, Norsk. Mag. f. Lægevidensk. **87**:194, 1926.

In an adult suffering from an obscure lung infection, dysuria was observed The urine contained no albumin, pus or blood. Casts were found, however. They were considered cylindrical bodies formed by the spores of a mold belonging to the species of *Penicillium*.

TOVERUD, Oslo, Norway.

Nervous Diseases

HEPATO-LENTICULAR DEGENERATION. STANLEY BARNES and E. WESTON HURST, Brain **48**:279, 1925.

The authors discuss four cases of extra pyramidal disease, in which cirrhosis of the liver was associated with gross damage of the lenticular nuclei. S. A. K. Wilson first described a series of such cases in 1912, and diagnosed them as "progressive lenticular degeneration." These authors believe that Hall's terminology — "hepato-lenticular degeneration" — is better, as it indicates "that the disease is associated with cirrhosis of the liver, and as this event is almost unique in neurologic experience, some suggestion of its presence would be better included in the title." After discussing their four cases at length, the authors concluded that: 1. Wilson's "progressive lenticular degeneration," Gower's "tetanoid chorea," certain cases of "pseudosclerosis" and Thomalla's "torsion spasm," should be grouped together as forms of "hepato-lenticular degeneration." 2. The nervous symptoms of this disease never occur until the liver has been grossly damaged. The hepatic cirrhosis seen at necropsy is an end-result of a series of attacks of acute hepatitis. 3. The toxin causing the hepatitis is not manganese. It probably has a bacterial origin in the alimentary canal. 4. The variation in clinical nervous symptoms depends partly on which regions of the lenticular nuclei are mainly damaged, and partly on the degree to which damage is done to other nervous structures. A very full bibliography is appended.

THE CENTRAL TRACTS OF THE NERVUS VESTIBULARIS. ISAAC H. JONES and WILLIAM G. SPILLER, Brain **48**:334, 1925.

The authors report a case of epidemic encephalitis in a boy, aged 15 years, the onset of which probably antedated death by more than a year. The follow-

ing points were noted: "Examination revealed an absence of vestibular function with no impairment of auditory function. A persistent spontaneous nystagmus existed, of a type suggestive of a central vestibular lesion. Examinations and tests were made just before death which occurred suddenly, and was probably attributable to the brain-stem lesion. The necropsy revealed nothing abnormal, thus indicating that there were no pressure phenomena and that the lesion was microscopic." The whole brain was removed and examined by one of the authors (Spiller), who found that there "was a limited area of complete degeneration in the center of the tegmentum extending from the lower part of the medulla oblongata well into the lower part of the pons, with the raphe as its center." Spiller concluded from his study that practically all of "the central tracts concerned with vestibular function pass through the area represented in this region. The radicular fiber of the nervus vestibularis and the nervus cochlearis escaped entirely. The generation involved only the central tracts of the vestibular system." A detailed description of the findings is given, as well as quotations from various authors, Winkler, Marburg, etc., photographs of some of the sections and a bibliography.

A Further Note on Hepato-Lenticular Degeneration. Stanley Barnes and E. Weston Hurst, Brain **49**:36, 1926.

The authors discuss here the findings on another of their patients who died after their former article (*Brain* **48**:279, 1925) was in press. They made a careful examination of the tissues, and here report on the changes found in the organs and the significance of the Kayser-Fleischer line (zone of corneal pigmentation). They believe that the corneal pigmentation may be deposited before the nervous symptoms have developed to the stage of observable clinical signs, and also that it never occurs before the liver is diseased. However, they feel that more accurate methods for recognizing early hepatic cirrhosis are needed to make this conclusive. Numerous illustrations of the sections and a full bibliography are given.

Lucas, San Francisco.

Pyelitis in Infancy—A Pathological Study. Bruce Chown, Canad. M. A. J. **16**:549, 1926.

The data for this study were taken from department of Pediatrics and of Pathology at Johns Hopkins Hospital for the years 1911 to 1924.

Twenty-nine case records of necropsies were analyzed; twenty-one were classed as acute or subacute and four as chronic. In four, no lesions were found as a source of pyuria; in one case there was a definite acute inflammation of the pelvis; in no case was there definite pelvic inflammation; in all cases with any urinary tract lesion there was a definite interstitial suppurative nephritis; in one case there was gross cystitis, with blocking of one ureter and interstitial nephritis; in fifteen cases the urine was cultured, in all of which a bacillus of the colon group was recovered. There was evident infection elsewhere in most cases, which was more frequently parenteral than enteral. The cases were equally distributed among the two sexes.

Microscopically, in the earliest cases are minute focal accumulations of cells, mainly polymorphonuclear, in the interstitial tissue of cortex or medulla. Pus cells are found in collecting tubules. As the condition advanced, some kidneys

showed diffuse inflammatory changes, intestinal and tubular, while other showed larger abscess formations.

The author concludes from the analysis of these twenty-nine necropsies, that the most likely route of infection is the hematogenous. He also concludes that the condition is as frequent in boys as in girls.

This conclusion seems hardly justified on the basis of twenty-nine cases of such severity as to come to necropsy, in face of the statistics based on the vastly greater number of mild cases seen in ordinary routine of practice.

The author also emphasizes the danger of erroneous diagnosis of inflammation based on necropsy, shedding of mucosa of pelvis, ureter and bladder, which he says is a normal condition.

MOORE, Omaha.

THE ALKALINE RESERVE IN SPASMOPHILIA. P. ROHMER and P. WORINGER, Rev. franç. de Pédiat. **1**:290, 1925.

Keeping in mind the recent work which has sought to establish a relationship between the calcium ion concentration and the acid-base equilibrium, according to certain mathematical formulas, the authors made a study of the alkaline reserve in cases of infantile spasmophilia. They found: (1) In cases of actual tetany, the alkali reserve was markedly diminished; this held true before, during, and after the active manifestations; (2) there was a slight lowering of the alkali reserve both in cases of latent tetany and in cases of rickets without spasmophilic symptoms; (3) under actinotherapy, the alkali reserve rose, and attained a normal figure after twelve to fifteen treatments.

LESLIE, Chicago.

THREE CASES OF SEROUS SPINAL MENINGITIS FOLLOWING INFLUENZA. J. L. BURKHARDT and J. KOLLARITS, Schweiz. med. Wchnschr. **56**:517 (May 29) 1926.

The authors report three cases of involvement of the central nervous system following influenza. The patients were boys, approximately 7 years of age, inmates of the Children's Sanatorium in Davos. The symptoms were as follows:

Case 1.—Elevation of temperature; equinovarus position during standing and lying down, during which the plantar reflex could not be passively compensated; increased tendon reflexes of the lower extremities with ankle clonus, priapism, pain on extension of the arms, with subsequent recovery.

Case 2.—Elevation of temperature; equinovarus position; increased tendon reflexes of the lower extremities; ankle clonus, priapism, photophobia, contractures of the thighs, improvement of contractures after lumbar puncture. Death resulted from pneumonia.

Case 3.—Elevation of temperature; equinovarus position with loss of passive motion of the feet; increased tendon reflexes of the lower extremities; ankle clonus; lumbar puncture showed increased pressure, the spinal fluid was sterile. After lumbar puncture there was a decrease in temperature. Recovery was complete except for partial ankle clonus.

ELTERICH, JR., Pittsburgh.

Diseases of the Ear, Nose and Throat

BEZOLD'S MASTOIDITIS AND THE BLOOD COUNT IN THIS DISEASE. L. H. KLEMPTER, Northwest Med. **25**:253 (May) 1926.

Bezold's mastoiditis is an abscess which breaks through the tip into the tissues of the neck, which occurs when the cortex of the tip and inner wall is thin, a condition frequently found in pneumatic mastoids. Klemptner reports three cases. He comments on the importance of a leukocytosis in making a diagnosis of mastoiditis.

SCOTT, Philadelphia.

Diseases of the Skin

LARGE SPORED RINGWORM INFECTION. MARTIN F. ENGMAN, Arch. Dermat. & Syph. **13**:352 (March) 1926.

By means of foreign protein (typhoid vaccine) injections intravenously in sufficient dose to produce a systemic reaction, Engman was able to cure large-spored ringworm infection in a short time. With other means of treatment this has always been a stubborn infection.

JEANS, Iowa City.

AN ISOLATED CASE OF ERYTHEMA ARTHRITICUM EPIDEMICUM. KATHERINE DODD, Boston M. & S. J. **194**:633 (April 8) 1926.

A white girl, aged 10 years, complaining of fever and headache entered the Harriet Lane Home of Johns Hopkins Hospital. The illness started three days before, when the child awoke with a wound on the little finger of the left hand which her mother attributed to the bite of a rat. The patient had vomited once; extreme anorexia was present, and she lay on one side with the eyes closed and breathing rapidly. She answered questions rationally but refused to move when requested; there was marked herpes labialis; the finger was tense and shiny. The following day, there was a widely distributed maculopapular eruption on the trunk, arms and legs, and some petechiae on the soles of the feet. Marked pain was present in all the limbs, especially in the left leg; there was no swelling or redness of the joints; the pains lasted over two weeks and the eruption about two days. On admission, the temperature was 103.8 F., pulse, 112; respiration, 32; the temperature remained high for five days, and was normal in nine days. White blood count, 14,400. Roentgenogram of the chest several days later showed that the "lungs were clear." "Two blood cultures, the first made on the day of admission and the second made five days later, after five days of growth, showed small greenish colonies, all deep in the plate. The colonies were composed of gram negative rods, varying in length from long filamentous forms to short, almost coccus-like forms. On these filaments appeared after many days of growth occasional swellings which were thought to be spores. The organism did not grow when transplanted in the more usual laboratory mediums, but grew well deep in ascitic agar. A third blood culture at the time of discharge was negative."

Reference is made to cases occurring in Haverhill, Mass., with similar findings but thought to be due to contaminated milk, reported in same journal, on Feb. 18, 1926, by Place, Sutton and Wilmer.

GENGENBACH, Denver.

ERYTHEMA NODOSUM AND LUNG TUBERCULOSIS. C. HAMBRO, Norsk. Mag. f. Lægevidensk. **87**:18, 1926.

Of 600 patients examined for various lung conditions, a history of erythema nodosum could be obtained in thirty-eight of the 426 patients with tuberculosis, whereas no such history was given by the seventy-four patients suffering from other lung conditions. Erythema nodosum is, according to the author, to be considered as pleurisy. It is an expression of a tuberculous infection of the organism.

The time elapsing between the attack of erythema nodosum and the symptoms of lung tuberculosis varies in this material from weeks to thirty-three years. In nine cases, however, erythema nodosum just preceded the pleurisy or the lung tuberculosis, and in seventeen patients the lapse of time was six months. The author emphasizes precautions in the treatment of erythema nodosum, and thinks it necessary to keep the patient under close observation the first one and one-half year after the attack. The convalescence period ought to be long, and in this way the author thinks it possible for some patients to escape the serious consequences of the disease.

TOVERUD, Oslo, Norway.

Surgery and Orthopedics

THE ROENTGEN ASPECT OF EMPYEMA IN CHILDREN. JOHN R. CARTY and CHARLES LIEBMAN, Am. J. Roentgenol. **14**:215 (Sept.) 1925.

The paper is based on 225 cases of empyema and 100 cases of nonpurulent effusion during thirteen years. The size of the chest permits a relatively small accumulation of pus, therefore, obliteration of rib outline is rare, and for the same reason obliteration of costophrenic angle is not common. A small collection will displace the mediastinum and produce early asymmetry of the chest and scoliosis of the thoracic spine. Differential diagnosis includes pericarditis, bronchiectasis, massive collapse, pneumonic consolidation, thickened pleura, and the important factor is the taking of pictures in both the erect and the prone positions. The authors find no increase in males as is the usual finding, and find the greatest incidence at 3 to 4 years of age with a rare subject under 1 year. The left side is most frequently involved with 3 per cent bilateral involvement, although others show as high as 8 per cent double empyema. Osteomyelitis is occasionally seen in postoperative cases, and thoracoplasty causes permanent marked deformity. The postoperative pictures made in a few subjects showed a remarkable return to normal.

STULIK, Chicago.

PROGNOSIS OF EMPYEMA. J. M. SMELLIE, Arch. Dis. Child. **1**:99 (April) 1926.

A study of thirty-six children, from ten to thirteen years after operation for empyema, shows that the remote prognosis is excellent. All show a negligible scarring.

PETERMAN, Milwaukee.

STRANGULATED RETROCOLONIC HERNIA OF THE ASCENDING COLON AND CAECUM, OPERATION, RECOVERY. WELLER VAN HOOK, Boston M. & S. J. **194**:534 (March 25) 1926.

A girl, aged 18 months, of average size and development, whose previous health was unusually good, was seized with severe paroxysmal abdominal pains, with no tumefaction felt in the morning, but late in the afternoon the bowels moved copiously with a small quantity of blood and mucus in the stool,

and tumefaction the size of a small tangerine orange felt in the right hypochondrium; the mass was not movable but was not adherent to the abdominal wall; visible intestinal peristalsis was present. The temperature was about 100 F. The diagnosis of intussusception was made, and an operation was performed the same evening. The mass was found to be a sac, the opening into which was visible, containing portion of the ascending colon, appendix and a few inches of ileum. The colon passed downward from the hepatic flexure and formed the anterior wall of sac, and then bending abruptly backward became itself the major part of contents of sac, and was slightly adherent to the posterior abdominal wall. With no difficulty nor questionable pulling, the sac was emptied by very gentle traction. The appendix was found to be slightly inflamed and was removed. The author believes it to have been due to an anomalous condition occurring prenatally as follows: "The caecum and ileum having begun their descent from the hepatic region, a slight premature agglutination took place between their coats and the posterior abdominal wall causing their arrest. The downward pressure on the colon coming from above caused the upper part of the ascending colon to glide down and fold over the caecum, with its appendix and a few inches of the ileum to be enclosed back of the colon in a well marked pocket or hernial sac."

GENGENBACH, Denver.

THE POSTOPERATIVE PULMONARY ABSCESS: A DISCUSSION OF ITS ETIOLOGY. EMILE HOLMAN, Northwest Med. **25**:290 (June) 1926.

Holman describes methods of attempting to produce pulmonary abscesses artificially. He comments on the failure to produce these abscesses by insufflation or otherwise introducing into the lung infectious matter. He contrasts the relative ease with which these can be produced by injecting septic emboli into the jugular veins. As to treatment, he advises early medical treatment by postural drainage; surgical evacuation before cavity walls become too firm, and against artificial pneumothorax in peripherally situated abscesses. He does not feel that bronchoscopic drainage is of very great value, except when the bronchus is obstructed. As to prophylaxis, he cautions against tonsillectomy soon after an acute infectious process.

APPENDICITIS IN AN INFANT. PAUL W. SWEET, Northwest Med. **25**:310 (June) 1926.

Sweet's patient was a girl, 16 months old, brought to the hospital with the parents' diagnosis of a "cold in the lungs." The physical signs and symptoms are not recorded, but the leukocyte count was 16,000, of which 90 per cent were polymorphonuclears. The abdomen was opened and a colon bacillus abscess was drained. The appendix was not removed. The child made a complete recovery.

SCOTT, Philadelphia.

THE OPERATIVE AND VACCINE TREATMENT OF CHRONIC OSTEOMYELITIS. V. KREISINGER, Cas. lek. Cesk. **64**:281-284 and 335-342 (Feb.) 1925.

The author reviews the progress of the surgery of osteomyelitis from the conservative removal of sequestrums to radical osteoplasty. In his twenty patients treated jointly with surgery and autovaccine, he has had fourteen cures and four unsatisfactory results. In the 217 collected cases, including twenty-

two with septicemia, 129, or 60 per cent cures are reported. Individual series of this group run up to 80 per cent cures with the combined method. The author feels that autogenous vaccines are much more potent than stock polyvalent vaccines.

STULIK, Chicago.

Miscellaneous

Bull. Soc. de pédiat. de Paris, Nos. 4 & 5 p. 79 (April 15) 1924.

J. Halle and Decourt presented a girl, aged 3 years, with psoriasis of the finger nails. The lesions were first noted at the age of 2 months. The appearance of a typical lesion on the child's abdomen made the diagnosis possible. The parents were suspected of syphilis, but the child showed no evidences.

L. Babonneix (p. 183) presented four children with optic atrophy and hereditary syphilis. The atrophy was attributed to a syphilitic basilar meningitis which involved the optic nerve.

J. Halle and Decourt (p. 188) presented an infant, aged 11 months, with urticaria pigmentosa. The eruption appeared at the age of 5 months, and covered the entire body with the exception of the face, feet and hands.

E. Cassoute and J. Rayband (p. 189) showed a girl, aged 9 years, with "sporadic" hemophilia. Hemorrhages began at 3 years. Horse serum, citrated whole blood, and peptone had no appreciable effect on the coagulation time.

Gelston (p. 192) discussed the incidence of tuberculosis in 2,500 California children from 1 to 14 years of age. Eight hundred and fifty gave a positive cutaneous reaction (34.5 per cent); 1,700 a negative reaction. Among the positive reactors, 28 per cent gave a family history of tuberculosis; 16 per cent of the nonreactors gave a positive family history. Of 835 children who reacted positively to the cutaneous tuberculin test, 151 reacted only to the human tuberculin, seventy-two only to bovine, and 612 to both.

Lereboullet and associates (p. 200) presented a girl with diabetes, who had been treated for one year. The weight had increased 8 Kg. and the glucose excretion in the urine had fallen from 154.40 Gm. per twenty-four hours to 0. The height remained stationary. All secondary symptoms disappeared.

Bull. Soc. de pédiat. de Paris, p. 207 (May 20) 1924.

J. Michaux and his co-workers cite several cases of varicella and herpes in an associated epidemic. The serums of two patients deviated the complement in both herpes and varicella.

L. Guillemot (pp. 211) presented an infant with hereditary syphilis who had been successfully treated with stovarsol.

J. Huber and R. Levassor (p. 212) showed a patient who developed a jacksonian convulsion and uremia in the course of pertussis.

J. Huber and R. Levassor (p. 215) presented an infant with massive hypertrophy of the right femur. The Wassermann test was positive.

Appert and Garcin's (p. 215) patient was normal until 9 years of age. She then moved into a "goiter valley," and after a year developed myxedema. The girl was 18 years of age but looked like a girl aged 12 or 13. Thyroid treatment produced good results.

G. L. Hallez (p. 217) supports the old belief that dentition may cause a severe general disturbance. He had two infants, aged 16 and 18 months, respectively, with high fever (40.5 C.), nervousness, and vomiting, all of which disappeared following incision of the gums. The fluid obtained at incision contained streptococci and *B. coli.*

R. Debre and his co-workers (p. 225) reported on measles at the Bretonneau Hospital (1922-1923). There were 355 cases with sixty deaths (forty-seven due to bronchopneumonia). Lesné (p. 230) reported 485 measles admissions at the Trousseau Hospital (1923) with 103 deaths (sixty-eight due to bronchopneumonia). The high mortality was attributed to association of the epidemic with influenza. Apert and Kermorgant had 673 cases of measles at the Hôpital des Enfants Malades (in nine months, 1922-1923) with a mortality of 16.4 per cent. J. Renault and R. Weismann-Netter (p. 240) reported a measles epidemic of nine cases in infants, aged from 2 to 5 months, after exposure. Eight infants died. Following a second exposure, all infants in the hospital were given from 3 to 5 cc. of convalescent serum and no cases developed.

Bull. Soc. de pédiat. de Paris Nos. 6 & 7 (May and June) 1924.

Marfan and his co-workers (p. 270) reported seven cases of craniotabes treated with ultraviolet rays. Consolidation occurred in from two to three weeks.

H. Dorlencourt and E. Spanien (p. 282) believe that dyspepsia due to fats does not indicate a lack of pancreatic lipase. An excess of fat is absorbed at the expense of the casein. In vitro, fat inhibits the digestion of albumins.

These authors (p. 284) found all infants with tetany or spasmophilia to have low blood calcium, from 6.9 to 8.8 mg.; infants with latent tetany had blood calcium levels of 8.8 to 10.3 mg. There might be hypocalcemia without tetany but the reverse was not found. The phosphorus was low in tetany but normal or increased in latent spasmophilia.

H. Lemaine and Cochez (p. 288) reported a girl, aged 9 months, who had eleven spontaneous fractures. The calcium and phosphorus were normal.

M. T. Urmana of Bogota stated that the incidence of acetonemia was high in his town (2400 meters above sea level). He had seen 61 cases of cyclic vomiting in the last few years. There were 19 deaths. All cases showed a marked ketosis and acidosis and an hepatic insufficiency. Symptoms and treatment were given in detail.

Génévrier and Breuniel (p. 311) observed an arterial hypertension (110 to 115 mm.) in congenital syphilitic subjects who had anemia, retarded development, and undernutrition.

Debré and his co-workers (p. 314) presented an infant who was normal at birth and up to 11 months. Convulsions were followed by blindness; idiocy and oxycephaly were present at the age of 20 months.

Dayas and his co-workers (p. 320) reported two cases in children, aged 8 years. Sudden abdominal pain, fever, vomiting and peritoneal facies were followed by death. Necropsy showed collections of ascarides in the cecum and large intestine. The appendices appeared normal.

Lesné and Lévy (p. 342) saw a boy, aged 9½ years, who had received diphtheria antitoxin one year previously. Following raw horse flesh with his meals, urticarial lesions — simulating beginning abscesses, appeared. One cubic centimeter of diphtheria antitoxin subcutaneously produced a serous orchitis in three days. The same serum minus part of its albumins produced no symptoms.

Bull. Soc. de pédiat. de Paris, Nos. 8-9 (Oct. and Nov.) 1924.

Leenhardt and Sentis (p. 347) reported the case of a girl, aged 14 years, who acquired a bacillary septicemia suddenly after a cold bath. There was a complete paraplegia, sensory and motor, but no fever, and the spinal fluid was normal. Nine months later, a Brown-Sequard syndrome was found with

a paraplegia in extension, much more marked on the left. Head zones of cutaneous sensation established the level of the spinal lesion at the ninth thoracic vertebra. Lipiodol (1.5 cc.) injected to confirm the level of the transverse myelitis produced a severe meningeal reaction with high fever. Death followed in one month.

J. Cathala and Lelong (p. 349) presented a girl, aged 10 years, who developed a left sided hemiplegia following a fall. Two years later, jacksonian convulsions began and gradually increased in severity. (There was every evidence of a central lesion in the brain.) After a severe attack of tonsillitis, the child expelled two ascarides by mouth and there were no more convulsions.

Nobécourt and his co-workers (p. 353) observed a girl, aged 13 years, who had persistent vomiting with malnutrition. Physical examination was entirely negative. Radioscopy revealed a megesophagus, or a dilatation of the entire esophagus. Esophagoscopy showed no stenosis of the cardia. Rapid recovery followed rest in bed and proper diet.

Bigart, Schreiber and Bonnet (p. 357) reported a case of pulmonary tuberculosis with cavity formation. The patient completely recovered four years after artificial pneumothorax.

Armand-Delille and his co-workers (p. 359) presented three cases of tuberculosis in older children who had made good recovery following pneumothorax.

P. Lereboullet and Joannon (p. 361) reported that, in 1923, sixteen patients of 180 admissions developed measles. After convalescent serum was used, four of 110 patients developed the disease.

Nobécourt (p. 366) treated three diabetic children (aged 11, 12 and 14¼ years, respectively) with insulin. All three made good progress and gained weight.

H. Lemaire and Cochez (p. 369) saw an infant aged 6 months, who developed scurvy and cutaneous and pulmonary tuberculosis while on sterilized milk. Orange juice caused no change until the sterilized milk was discontinued. With fresh milk, meat juice, etc., recovery took place.

Roederer (p. 394) presented a case of congenital elevation of the scapula producing a scoliosis. There was a supernumerary half vertebra between the seventh cervical and first thoracic vertebrae. There were also six lumbar vertebrae with a spina bifida occulta.

Ribadeau-Dumas and Fouet (p. 410) proposed the use of an aminoserum in the disorders of nutrition. In confirmed athreptic conditions, the functional deficiency of the tissues causes an alimentary intolerance, especially for proteins and fats. The cell metabolism is unable to take care of the daily requirements and those for growth. Saline and glucose solutions have not been satisfactory, since the fluid injected is not retained in the tissues but is rapidly eliminated by the kidneys. The glucose causes a transient hyperglycemia and is recovered in the urine. The fluid mass in the circulation is temporarily increased but the nutritive processes and tissue repair are not at all influenced. Five years previously the authors, treating infants with antipneumococcus serum, noted a permanent increase in body weight even in cases with digestive disturbances. The permanent weight increase, contrary to the transient increase after introduction of fluid seemed to indicate a true organic fixation of the serum introduced, an assimilation in whole or of parts. It could not be an assimilation of the mineral salts with a fixation of water, since horse serum contains a small amount of salts. The serum, however, is rich in proteins, 44 Gm. of serum albumin and 30 Gm. of serum globulin per liter. These proteins

contain a large amount of amino-acids which by their chemical character might be easily assimilated by the recipient organism. Van Slyke and Meyer, Henriques and Andersen, and others, have shown that a positive nitrogen balance and good nutrition might be attained by the intravenous introduction of amino-acids. The experiments seemed to indicate that most of the amino-acids introduced were only slightly toxic, and that the recipient organism was capable of absorbing and synthesizing the acids into tissue. The composition of a solution for parenteral feeding was attended with great difficulties, but the possibilities were enticing. Abderhalden had shown that the artificial mixture of all the amino-acids composing a proteid could replace the proteid, but the mixture could not be made without great care. Although it was known that tyrosin, tryptophane, and lysin were essential, the cytogenic value of the different proteins was extremely variable. It was necessary to offer the organism a choice of various amines in abundance. The fate of the introduced proteins remained obscure. The albumins might remain in circulation, at least they were not necessarily transformed into protoplasm. A mixture of amines isolated from the casein of cow's milk was used. The composition was: alanine, 0.9; leucine, 10.5; serine, 0.2; glutamic acid, 11; aspartic acid, 1.2; arginine, 4.8; lysine, 5.8; histidine, 2.6; cystine, 0.7; tyrosine, 4.5; phenylalanine, 3.2; proline, 3.1; tryptophane, 1.5. The addition of this mixture to antipneumococcic serum in the proportion of 1 to 2 per cent had no advantage over the use of pure serum, and did not protect against serum sickness. Glucose serum isotonic) was then adopted as a vehicle. Later, a partially disalbuminized serum was used which prevented serum sickness. Daily doses of 30 to 100 cc. of 3 per cent solution were given. There was no local reaction and absorption was normal. A slight elevation of temperature for several hours (to 100.4 F.) with a trivial reaction followed injection. No harmful results were seen. The influence on the body weight and the improvement, especially in acute dehydration, were very good.

E. Lesné and C. Richet (p. 414) used an amino-serum prepared by Robert and Carrière. The serum, glucose, 4:1,000, or sodium chloride, 7:1,000, contained 40 Gm. of amino-acids per liter. Fifty cubic centimeters was given by proctoclysis daily for several days. Three patients were treated, one with apparent success. The authors tried subcutaneous and intravenous injections in adults, but encountered serious symptoms of shock and syncope. However, they felt that the treatment was capable of giving good results, and that amino-serum therapy should be introduced into therapeutics. The serum should have a definite constitution; the chemical nature of the acids must be exact.

PETERMAN, Milwaukee.

PHYSICAL EDUCATION IN THE PUBLIC SCHOOLS OF PORTO RICO. E. M. IRVINE-RIVERA, Porto Rico Health Rev. **1**:10, 1926.

The department of physical education, established in 1912, has been systematically developing this phase of school life. It now recommends that no school site should be accepted by the Board of Education which is not large enough for the building and playground. In addition to drills and exercises, particular emphasis is placed on organized games, with the result that the development of a spirit of good sportsmanship and fair play is becoming an important part of school life.

LESLIE, Chicago.

BERIBERI CONTROL FROM AN ADMINISTRATIVE VIEWPOINT. J. W. H. CHUN and WU LIEN-TEH, Nat. M. J. China **12**:9, 1926.

The theory generally accepted is that beriberi is due to a deficiency in the diet. These authors cite other views, but believe these factors will usually be found associated with a faulty diet. They discuss these in detail: deterioration of rice during storage, loss of vitamins through improper preparation of the rice, importance of a correct correlation between the whole diet and the vitamin content and individual factors which favor the onset of beriberi. They believe that a combination of legislative and educational measures are necessary to the prevention of beriberi. Legislative measures might provide undermilled rice for public institutions and the subsidizing or establishment of rice mills which will produce proper rice. The public must be educated to the realization of the advantages of undermilled rice, hygienic living conditions and vitamin-containing foodstuffs. Given sufficient quantities of the last named, the disadvantages of white rice will be avoided. A full bibliography accompanies the text.

LUCAS, San Francisco.

Society Transactions

AMERICAN PEDIATRIC SOCIETY

Thirty-Eighth Annual Meeting, held at Niagara Falls, Canada, May, 1926

(Continued from page 320)

SECOND SESSION

J. H. Mason Knox, M.D., *in the Chair*

Observations on the Gastro-Intestinal Gradient and the Autonomous Nature of the Intestinal Musculature, with Reference to Their Practical Application in Clinical Medicine. Presented by Dr. D. M. Cowie, Dr. J. P. Parsons (by invitation) and Dr. F. H. Lashmet (by invitation).

This was a lantern slide demonstration, considering the history of the subject with particular reference to the work of Gaskel on the heart gradient in 1883, and of Alvarez on the gastro-intestinal gradient in 1913 to date. Attention was called to the autonomous nature of the circular and longitudinal muscle, as proved by the removal of the fibers of Meisner's and Auerbach's plexuses, and to the supposed controlling effect of these plexuses. Reference was also made to the peculiar area of tissue on the lesser curvature of the stomach near the cardia, where a pacemaker for the gastric gradient is thought to exist.

These observations confirm the work of Alvarez, and add a few additional facts. It was pointed out that with the proper selection of the animal and proper conditions as to temperature, oxygen supply, and immersing solution, there is a characteristic rate, tone, amplitude, and metabolic gradient in the intestinal tube. That is, the duodenum beats fastest and the lower segments at a decreased rate, or inversely as the distance from the duodenum. The tone gradient shows the same characteristics while the amplitude gradient is opposite, that is, the amplitude of contraction seems to increase as the distance from the duodenum. No intact animal experiments were reported.

The effect of infection on the intestinal gradient was illustrated by a case of snuffles in a rabbit. In this rabbit there was a mixed gradient; the upper ileum beating slower than the lower ileum, and a change in the amplitude. Attention was called to the effect of toxins on the gradient as pointed out by Alvarez, and to the possible benefit that may accrue to patients with infectious diseases in which distention often becomes a distressing symptom, if we knew which segments were particularly acted on by the toxin, and how these segments might be brought into line by the action of some specific chemical substance or organic extract.

The effect of acids, butyric, acetic, lactic and hydrochloric, in high dilutions was demonstrated. Of particular interest was the difference with which they characteristically act on the different intestinal levels or segments. The differing effects were shown of calcium chloride and calcium lactate, when one salt is almost completely disassociated or ionized and the other is not.

Gallbladder bile in high dilutions was shown to depress the tone of all segments. The duodenum tone is affected first, then in order, the upper ileum, lower ileum and colon. The rate and amplitude were also characteristically altered. Macdonald liver extract first momentarily lowers the tone of all segments, then greatly increases the tone and amplitude with a tendency

to throw the lower ileum into tetany. This is quickly overcome by the addition of a very small amount of gallbladder bile.

Sodium taurocholate, sodium glycocholate, and ox bile (synethetic) act the same as bile, while cholin hydrochloride and guanidine resemble Macdonald liver extract in their action on the contracting intestinal segments. Hypertonic saline solution throws all segments into tetany.

The well known effect of epinephrine and pituitary extract on an intestinal segment was shown. But it was also shown that they react differently (quantitatively) to the various segments.

The possibility of heightening the gradient and establishing onward, downward peristalsis was discussed, and reference was made to conditions in which this principal may be utilized from the standpoint of treatment of gastro-intestinal upsets in infant, child or adult.

The method of study was illustrated by a motion picture of segments of the duodenum, upper and lower ileum, contracting in Locke's solution and recording on the chymograph. In this demonstration, the effect of calcium chloride and Macdonald liver extract was shown.

DIGITALIS THERAPY IN CARDIAC DECOMPENSATION IN CHILDREN. Presented by DR. WILBURT C. DAVISON and DR. A. WILMOT JACOBSEN (by invitation).

On the assumption that the usual ineffectiveness of digitalis in children was due to inadequate doses, large amounts of the dried leaves of digitalis were given to sixteen children suffering from rheumatic heart disease who were orthopneic and edematous, and the administration was continued until definite effects were obtained. The criterion of the desired effect of digitalis therapy was a loss of edema, and nausea or marked slowing of the pulse was considered as a sign of complete digitalization. From 0.3 to 1.06 grains of the dried leaves of digitalis per pound of body weight (an average of 0.5 grains per pound) were required for complete digitalization. This amount is more than twice the dose which is usually effectual in adults. As there is this great variation, the "human unit" rather than the "cat unit" should be considered, and the individual tolerance of each patient should be determined by giving 3 grains of the drug every six hours until nausea or marked slowing of the pulse develops (usually after 4 to 8 doses). The dose should then be decreased to 1½ grains twice a day, as this amount is equivalent to the usual daily excretion of the children in this series. However, should nausea or marked slowing of the pulse develop while this reduced dosage is being given, digitalis should be discontinued and not readministered until one to two days after all symptoms of intoxication have disappeared. The administration of digitalis in these amounts to edematous children suffering from rheumatic heart disease usually causes a loss of edema, an increase in the patient's comfort and, in comparison with the fate of ten children who did not receive the drug, a reduction in mortality.

DISCUSSION

DR. MCCULLOCH: Dr. Davison has directed attention to three signs produced by the administration of digitalis, namely, nausea and vomiting, a drop in the pulse rate and loss of edema. To this I would add a fourth, the downward deflection of the T wave in the electrocardiograph. This is an early sign, and usually appears about or before the time the pulse rate drops. These two signs occur before vomiting appears. The Eggleston dosage can be relied on in estimating the amount of the drug to be given for a toxic effect.

The drug varies in its power to produce a toxic effect as do the children in their reaction to the drug. If the drug is purchased from various sources, the response may vary a great deal. A number of recent investigations show this to be true. The size of the dose to be given depends on the rapidity with which one wishes to get an effect. If one gives it in acute cardiac failure, the rapidity of response varies a great deal, but if there is a period of rest preceding the administration of the drug the response will be more constant. I think that Dr. Davison's idea of giving 0.3 grains every six to eight hours is a safe procedure. By following this plan one is not likely to give an overdose.

DR. DAVISON: Changes in the electrocardiogram are, of course, a definite indication of the absorption of digitalis, but are not as constant an index to its therapeutic effect as are clinical symptoms. The amount of digitalis per pound of body weight required to cause an alteration in the T wave varies in different persons, and this quantity is often insufficient to produce the desired clinical effect. Therefore, it is really more accurate as well as much simpler to use nausea as a criterion than to obtain electrocardiographic records at frequent intervals. For patients who have been vomiting before digitalis therapy is begun, and who consequently cannot retain the drug if administered by mouth, 30 minims of the tincture of digitalis diluted with 1 ounce of physiologic sodium chloride solution may be given by rectum every six hours until the pulse rate is definitely reduced (usually after four to eight doses). The amount should then be decreased to 15 minims of the tincture diluted with 1 ounce of physiologic sodium chloride solution twice a day to replace the daily excretion. As vomiting obviously cannot be used as an index of the effect of digitalis in these patients, the pulse rate must be measured at intervals of four hours. This rectal dosage is equivalent to that outlined for oral administration, and the results obtained in patients to whom digitalis has been given by rectum indicate that the drug is equally well absorbed and tolerated. Preliminary rest in bed does not seem to be of any advantage for, as the charts indicate, one of the children gained 7 pounds and another patient gained 11 pounds of edema while resting in bed before digitalis therapy was begun.

CONCENTRATED FEEDING IN CHILDREN ABOVE THE AGE OF INFANCY. Presented by DR. HENRY HEIMAN, New York, and DR. PHILIP COHEN, New York (by invitation).

Concentrated feeding has proved successful in infancy. Formulas of relatively high caloric values have been frequently devised with good results, such as Keller's malt soup mixture, the Czerny-Kleinschmidt butter-flour mixture, Schick's whole milk and added sugar formulas (dubo, etc.), and whole acidified milk with added sugar, best associated in this country with the name of Marriott. As a standard of concentration we have chosen the one of Pirquet, the caloric value of milk, or 20 calories to the ounce. For all formulas having a fuel value greater than this, such as those enumerated, we have reserved the term concentrated feeding.

Except for cereals there is little mention of foods other than milk being concentrated, yet we meet many children over the age of infancy who do not gain properly and for whom a concentrated diet would be a boon. There is, especially, one type of child who can eat well of a limited quantity of food, which in the usual diet is of unsufficient calories to cause a gain in weight. If the food is concentrated, then the limited volume intake will yield the normal number of calories. A child who is hyperactive or a child who is thin because

of an abnormal metabolism may also require a concentrated diet to compensate for a relatively limited volume intake.

Following the plan of Schick at Mount Sinai Hospital, New York, we have concentrated every article in the diet of such children. By adding flour, sugar, fats, oils, and other naturally concentrated foods in various recipes we have often been enabled to supply twice the amount of calories a similar bulk normally contains. In addition, we recommend foods of naturally caloric value, such as cream, butter, bread and vegetables of the highest carbohydrate content.

We have pursued this plan in about 200 subjects, with the opportunity to follow up over eighty-five. We were able to check losses in weight or improve the nutrition in 50 per cent of our cases, a better result than we could obtain with previous methods.

DISCUSSION

DR. SCHICK: I am particularly interested in the question of concentrated feeding. If we compare the concentration in caloric value with milk according to Pirquet's system of nutrition, we find that the infant in the second part of the first year starts to take more concentrated food. After the first year of life, the entire food and water intake of the child is approximately one and a half concentrated.

If we encounter difficulty in feeding, we have to resort to concentrated feeding. Every physician has, at times, ordered more concentrated food, that is, the use of more fats and carbohydrates in the preparation of dishes. It is important to remember that concentrated feeding does not mean that food alone is to be given with no fluid whatsoever. If the desired caloric intake is accomplished, we then can always give water or other fluids besides. This is especially necessary in summer and in cases of fever.

DR. HOOBLER: Was any attempt made to balance the food?

DR. BLANCO: Have you had any difficulty with the fats in using concentrated food?

DR. HEIMAN: Do you mean concentration as estimated in calories per pound or the food ratio?

DR. HOOBLER: I referred to the percentage of protein, carbohydrate and fat.

DR. HEIMAN: We do have the food factors balanced. We have 15 per cent protein, 60 carbohydrates and the balance fats. With reference to the neuropathologic cases, these are the most difficult to feed, so we do not attempt to give them fats, but simply proteins and carbohydrates.

CERTAIN BIOLOGICAL PROPERTIES OF HUMAN MILK. Presented by DR. B. RAYMOND HOOBLER, JULIA OUTHOUSE (by invitation) and ICIE G. MACY, Ph.D. (by invitation). From the Nutrition Research Laboratory, Merrill-Palmer School and Children's Hospital of Michigan, Detroit.

Through the cooperation of the Detroit wet nursing bureau, a composite sample from all the mothers delivering milk to the bureau was made available for this research. The number of women on the bureau varied from ten to sixteen in number. The milk, collected under the precautions laid down by the bureau, was pooled in analogous proportions, bottled, sealed air tight with paraffin and delivered fresh to the laboratory daily. No effort was made to control the diets of the wet nurses other than the supervision already in vogue at this bureau, which, in general, consisted of a generous mixed diet with

ample fruits and vegetables. No food rich in any particular type of vitamin was prescribed, and none of the mothers at any time during the observation took any cod liver oil.

A large colony of healthy rats was fed on a purified basal ration. At the beginning of the experimental period, the young animals were placed in separate cages in which individual food records were obtained. In every instance the vitamins and the human milk were fed fresh daily in separate dishes from the basal ration, so that very accurate intake could be recorded of the various food elements.

In the vitamin A experiments, the basal ration was irradiated with the Hanovia quartz mercury lamp for thirty minutes at a distance of 15 inches to furnish the antirachitic factor. Vitamins B and E, respectively, were supplied by Harris yeast and ether extract of wheat germ. Likewise in vitamin B studies, 5 drops of cod liver oil and 2 drops of wheat germ oil supplied the vitamins A, D and E.

In vitamin B experiments, the animals were kept on raised screens throughout the period of observation in order to prevent the ingestion of feces, which precaution we believe necessary to obtain perfect results.

In all our observations, positive and negative controls have been included in the series; protective as well as curative experiments have been performed. Daily routine vaginal smear examinations have been made, and whenever possible the ability of the female to bear and rear normal young have been taken as a crucial test.

EXPERIMENTAL RESULTS

Vitamin A in Mixed Human Milk.—Human milk, as is true of cow's milk, is relatively richer in vitamin A than in vitamin B.

The vitamin A content of 2 cc. of mixed human milk was sufficient to prevent the development of xerophthalmia in rats on a diet otherwise free from vitamin A. The growth factor was as perfect on 2 cc. as on those fed on as high as 15 cc. of human milk daily.

It has been shown that vitamin A may be stored in the body to a considerable extent, and be drawn on when the animal is placed on a diet slightly deficient in vitamin A.

Two cubic centimeters of mixed human milk as the only source of viatmin A was sufficient for female rats to successfully rear normal young, but it was observed that the young rats whose maternal parents received this small quantity had very little vitamin A stored in their reserve depot, since these young rats developed xerophthalmia on a vitamin A free diet in eighteen to twenty-two days, whereas the young of the normal rats on regular stock breeding ration do not exhibit vitamin A deficiency until five to six weeks on a vitamin A deficient diet.

Vitamin B in Mixed Human Milk.—In no instance in these studies has it been possible to secure normal growth and physiologic behavior when 5, 8, 10 and even 12 cc. of mixed human milk served as the only source of vitamin B in a diet otherwise adequate, whereas in quantities of 14, 15 and 16 cc. daily, subnormal gains were made, but it was not until 18 and 20 cc. of milk were given that continued growth approximated the normal. When these levels were increased progressively to 25, 30 and 35 cc. daily, simultaneous increments of growth and basal food intake resulted. As a rat increases in weight the need for a greater quantity of vitamin B is apparent, which substantiates the findings of Cowgill. There is a tendency to delayed sexual maturity in the females on milk levels below 18 cc., and normal ovulation has taken place only when a minimum of 20 cc. of the mixed human milk served as the daily

source of vitamin B, and not until 25 to 30 cc. was fed were the females able to produce their young. But even on these high levels the mothers were not able to feed their young, lactation being unsuccessful, and the young either died before 21 days of age, or they ultimately developed the usual symptoms associated with vitamin B deficiency.

COMMENT

From the data presented, it is obvious that the average mixed breast milk is a relatively rich source of vitamin A in contrast to that of vitamin B (2 cc. being sufficient for vitamin A and 25 to 35 cc. for vitamin B). From these observations, it seems certain that there is a relatively large storage of vitamin A in the body, and it likewise seems certain that a mother may create a store of this vitamin in her offspring, providing the mother's diet is ample in quantity of vitamin A.

The vitamin B potency of mixed human milk is extremely low. The body is not able to store any appreciable amount nor is it able to synthesize vitamin B. The mother's ability to supply it to her offspring is dependent on the vitamin content of her food supply.

The child has little margin of safety in respect to its vitamin B requirement both during its prenatal existence and its suckling period, even though the mother's diet be adequately planned.

PRACTICAL SUGGESTIONS

1. It is extremely important that the diet of the pregnant woman be carefully supervised as regards its content of all vitamins, not only for her own well-being but for the welfare of her unborn child. By doing so, it may assist her (1) in producing milk more suitable for the growth of her child; (2) she may thereby store up in her offspring a vitamin available for emergency should maternal milk fail; (3) it will protect the offspring during its fetal period from the effects of a deficiency of vitamin, the full consequences of such deficiency being yet unknown.

2. From the relatively small amount of vitamin B in human milk, we may well concern ourselves with the possibility that many nursing mothers do not supply sufficient of this growth producing element to their babies. This suggests that during the lactating period the mother should be supplied with ample vitamin B food and, in addition, spoon feedings of material rich in vitamin B should be given the infant as a safeguard against a low vitamin B in mother's milk; this should be done early in the nursing period. Since cow's milk is equally poor in vitamin B, artificially fed babies should be likewise protected.

HUMAN AND COW'S MILK IN THEIR RELATION TO RICKETS. Presented by DR. ALFRED F. HESS.

As infants can be nourished only on milk, this food is of prime importance in the study of rickets. Undoubtedly human milk is superior to cow's milk in preventing rickets. However, it is inadequate as a preventive, as one-third to one-half of breast fed infants develop rickets to some degree. Experimental tests on rats of human and cow's milk showed that human milk in per capita doses of 20 to 25 cc. possessed no antirachitic properties. From such experiments it would seem evident that the preventive value of human milk in rickets

cannot be due to its content of antirachitic factor for the rat is the standard animal for testing this nutritional factor.

Experiments on the cream of cow's milk showed that the antirachitic factor is present almost entirely in the cream. Eight cubic centimeters of cream sufficed to protect rats from rickets. This was not due to vitamin A, as the potency of the cream was not reduced following oxidation. Peculiarly enough, an equivalent amount of "upper third milk" containing the same amount of fat did not protect the rats. These experiments would seem to show that 20 per cent cream may be of value in the feeding of infants, and, second, that skimmed milk may contain some rachitogenic factor.

Although cow's milk may be improved by having the cows out at pasture, such milk does not develop sufficient antirachitic properties to protect the infant. In order to bring this about, the milk itself will probably have to be irradiated.

It was found that the antirachitic potency of human milk could be greatly enhanced if the woman is irradiated for a short time. For example, in one instance in which 25 cc. of human milk failed to show any curative properties, it was able to bring about an absolute cure after the woman had been irradiated by ultraviolet light. This suggests that nursing mothers be irradiated in this way in order to protect their infants from rickets. Such treatment may likewise protect women from the excessive withdrawal of calcium and phosphorus which accompanies lactation.

THE PRODUCTION AND HANDLING OF HUMAN MILK. Presented by DR. HENRY DWIGHT CHAPIN, New York.

The production and handling of human milk by the children's welfare federation of New York was started on Oct. 6, 1921. From that date to May 1, 1926, 5,296 quarts have been produced and distributed by this agency. For the first three years only one station was in existence, but since then three stations in different sections of the city have carried on the work. The only milk accepted is that expressed in the stations under the eye of the matron in attendance. It is astonishing how much milk can often be secreted when the breast is properly handled. One mother supplied us with milk for eleven months, frequently giving us 40 ounces a day, as well as completely satisfying her own infant. Another mother, aged 26 years, has now three children—the oldest 4½ years, the second 2 years, and the third 6 months. She has nursed these three children who are pictures of health, and at the same time sold to the federation 400 quarts of her extra milk, which has netted her an income of over $1,700 during the four years. Lactation can be prolonged to the fifteenth and even the eighteenth month, and the composition of the milk varies little from the earlier to the later period.

The technic of collection is as follows: The breast is not drained for an hour before coming. The mothers are taught to wash their hands with running water and soap before expressing their milk; the matron washes her hands with running water and soap, then cleanses the mother's nipples with boiled water and cotton pledget, one nipple at a time, the matron not permitting the mother to express milk from a nipple that has been touched by her clothing until again cleansed. A clean towel is tucked in the clothing under the breast, also covering the lap, and a sterilized graduate is placed on her lap. The mothers become very efficient in stripping their own breasts. No pumps have been used. The milk is transferred from the graduates to sterile bottles, pooled, and placed in the refrigerator for distribution into smaller sterile

bottles on receipt of orders. No physical examination of the mother is made, and no special diet is recommended other than plain nourishing food. A specimen of pooled milk is analyzed every month. These analyses show that the fat, protein and lactose are fairly uniform when the milk is thus collected and pooled, and in this way is similar to the herd milk of cows. Bacterial counts made by the Health Department Laboratory a few hours after collection showed an average of 12,550 colonies per cubic centimeter; after twenty-four hours' standing in an icebox at 45 F., an average of 38,425 colonies, and after forty-eight hours, 3,580,500 colonies per cubic centimeter. Pasteurized specimens average about 100 colonies per cubic centimeter. Experiments on the keeping qualities of the milk seem to show that human milk acts much as cow's milk under similar conditions. Purchasers, heretofore, have been directed to pasteurize the milk at once, this being stressed as no Wassermann test is made, but recently, as the demand is very irregular, we have decided to pasteurize the milk ourselves. During 1925, 170 babies were supplied by the federation; to some of these babies this milk offered the last chance for life. The plan of furnishing human milk should come to stay, as it is the only practical way of reducing much of the early infant mortality. The charge for the milk is 25 cents an ounce for those who can pay this amount, 15 cents an ounce to hospitals, and about one-fourth of the milk collected is given away to needy and desperate cases.

DISCUSSION

DR. F. W. SCHLUTZ: The interesting fact brought out by Dr. Hoobler is the marked inadequacy of vitamin B in breast milk. It is astonishing that this important factor should be so lacking in breast milk and that apparently it is difficult to store it. It is probably not altogether an accident, but rather an expression of the fitness of our environment that this particular element is so prevalent in nature.

It is interesting that Dr. Hoobler has been able to confirm what has been known for some time from the agricultural experiment; namely, that vitamin B can be increased in the milk of the lactating animal by giving food rich in this factor. Leafy green vegetables contain it particularly. It is obvious that they should form a generous part of a nursing mother's diet.

The experiment of Dr. Hoobler also affords proof of the advantage of giving such food even to the young nursing infant. It should do away with the apprehension felt in some quarters regarding the early use of such foods in infant feeding, as it is both a safe and a correct procedure.

DR. GERSTENBERGER: I wish to discuss Dr. Hess' paper. With the permission of the President and with the sanction of Dr. Hess, I shall show you some slides which will give some information which we have obtained, bearing on the antirachitic power of human milk. For some time we have been interested in this problem, but have attacked it in a different manner than has Dr. Hess. To wet nurses and to some mothers, one tablespoon of cod liver oil was given daily and the milk produced by these women was fed to rachitic infants, in some cases from the bottle and in other cases directly from the breast. A year ago we observed two subjects, on one of whom the breast milk, after seventy-six days trial, produced no improvement neither by roentgen-ray diagnosis nor by blood chemistry studies. In the other child, the bones went on to nearly complete healing at the end of seventy-five days of feeding. This infant received its milk directly from its own mother, and it was therefore thought possible that the raw breast milk was superior in this respect to that of the wet nurses, which had been canned. However, on the basis of observa-

tions that have been made in the clinic since that time, we are, in retrospect, convinced that the healing which occurred in this child was not due, in the first place, to the raw state of the breast milk, nor in the second place, to the breast milk itself, but to the activity of the antirachitic factor applied in some form or other before admission to the hospital. This explanation has been substantiated by the observations that have been made in our clinic during the present year. The roentgen-ray records of the child who improved on its own mother's milk during June, 1925, showed signs of healing when the first roentgenogram was taken during the first week after admission. As just stated, we know now that the antirachitic factor cannot produce changes so quickly in the roentgen-ray plate unless the rickets is in the stage of healing. The infant who improved on its mother's breast milk gained slightly in weight, whereas the other gained somewhat more. Of the subjects studied during the present year, none showed improvement after breast milk.

In order to be sure that improvement that follows the use of the antirachitic factor in some form is not due to the application of the antirachitic factor before the material to be tested is used, it is necessary, Dr. Hartman, Dr. Wilder and I learned, to keep the infant for at least five weeks on a food that is known to contain no antirachitic substance and in an environment that is free from this factor. One of these infants, therefore, was fed lactic acid milk for thirty-eight days, another, casein milk for forty-eight days and a third, lactic acid milk for sixty-seven days before the breast milk observation was begun. In the first infant, the breast milk was offered over a period of forty-five days; in the second, over one of thirty-three days, and in the third over one of thirty-six days. In none was any improvement noted in the roentgenogram nor by a phosphorus curve rise. In each case, however, improvement, both in the blood and as shown by the roentgen ray, even though the weight curve rose in each instance, occurred on the twentieth day of feeding of protein S. M. A. in the first case; on the twenty-ninth day of feeding of S. M. A. in the second case, and on the thirty-second day of the feeding with S. M. A. in the third case. Consequently, we are convinced that human milk does not contain enough of the antirachitic factor to cure rickets nor to prevent it, even though the women producing the milk received 1 tablespoon of cod liver oil daily. The amount of cod liver oil that is required to cure rickets is very small, and paradoxical as it may seem, less than that needed to prevent it. We will soon have occasion to present what we think are convincing data of the correctness of our conclusions.

Five slides were shown.

Dr. Alfred F. Hess: How do you explain the fact, that you found ten or twelve times as much vitamin A as vitamin B? It is believed that these vitamins cannot be synthesized, that they are derived directly from foods. Is it that these women do not get enough vitamin B or that they use it up in their organism or that it is not secreted in the milk to the same extent as vitamin A? This result is just the opposite from what we believe, namely, that vitamin B is more widely distributed than vitamin A.

Dr. Herman: What has been done in New York with the production and distribution of breast milk is due entirely to Dr. Chapin's efforts in association with the children's welfare association. The success of the plan depends on the correct location of the stations for the collection and distribution of breast milk. The stations should be connected with those for infant welfare, and must be located in a tenement district where there are certain nationalities.

DR. HOOBLER: I want to congratulate Dr. Chapin on the growth of his work, which has been phenomenal.

It is still somewhat of a question in my mind as to the wisdom of taking milk from mothers who have not had the Wassermann test. I am not certain what effect pasteurization would have on the spirochetes in the milk. I do not know whether Dr. Chapin is informed on that point. In Detroit, we insist that every mother shall be Wassermann free and remain so. We also examine regularly for tuberculosis. We have made another innovation—we are using mechanical expression of the breasts with the Abt apparatus. It is difficult for the mothers to express the milk if they are not adept, and by manual expression the milk is more likely to be infected, especially as the hand becomes drippy and wet with the milk. With the Abt breast pump the milk can be secured under the most aseptic conditions, and constitutes what we call "certified breast milk" compared with the milk expressed by hand which gives a much higher bacteriologic count than that secured by means of the pump. We believe this milk, which we classify as "certified," can be given to babies raw, thus avoiding the change that pasteurization brings about, since we believe the less the change from normal mother's milk the better for the infant.

Detroit has reached its 100,000 ounces per year which I predicted it would do; we are handling about 8,000 to 9,000 ounces per month.

DR. SHERMAN: I have wondered how long it would be before we had an organization that would make a general distribution of breast milk and a financial success of such a project. I have here the figures from the Ingleside Home in Buffalo, compiled by Dr. Harry R. Lohnes, who started this certified human milk dairy farm. It is amazing the amount of milk that has been produced under his supervision, and the financial results that he has been able to show. The women are given all the tests, Wassermann, etc. They express the milk and throw away the foremilk so that there is no contamination. The Abt pump is used, and all possible precautions are taken to prevent contamination. Out of seventy women delivered during the past year, a daily average of fifteen gave breast milk. They have produced 42,598 ounces, of which 38,428 have been sold at prices from nothing to 20 cents per ounce. This milk not only helps the babies who receive it, but it is a good thing financially for the home and for the girls who contribute the milk. It has yielded the Home $2,873.42, and the girls $2,553.70 during the past twelve months. The milk is sold to hospitals for 10 cents an ounce, and runs up to 20 cents for outside patients. The girls received 6 cents per ounce, whether it is given away or sold. I am giving these facts to show that Buffalo has done something along this line. Dr. Lohnes is to be congratulated for his interest in expanding this business, from which he makes no profit except the good he accomplishes.

DR. MARRIOTT: I think we will all agree that milk obtained by nursing a healthy mother is the best possible food for a normal infant. Such milk is readily digestible, contains more calories to the ounce than most formulas of cow's milk in common use, and because of the fact that it comes directly from producer to consumer, there is little chance of bacterial contamination. Furthermore, an infant nursing at the breast usually takes more food than when given milk from a bottle. When breast milk is collected and distributed, many of its advantages are done away with. The milk is no longer fresh when delivered and may become contaminated by bacteria. It is given in carefully measured amounts, which may be insufficient for the infant, and altogether possesses little, if any, advantages over a cow's milk formula properly prepared and having the same number of calories per ounce. At one time in St. Louis

we collected a considerable amount of breast milk for distribution and use in the hospital, but after a thorough trial we were not convinced that the effort was justified or that the results obtained with the infants were any better than when given proper artificial formulas. By this I do not imply that artificial feeding is as good as maternal nursing, but the feeding of breast milk from a breast milk "dairy" is a very different thing from maternal nursing. I should like to ask Dr. Chapin what he considers the particular uses and advantages of the milk collected and distributed under the plan he has described.

DR. KNOX: I should like to ask Dr. Hess what, in his opinion, is the comparative value in increasing the vitamins of heliotherapy as compared to ultraviolet light or other artificial rays.

I understand that the surgeons feel that heliotherapy is much more potent in promoting the healing of wounds and in the treatment of bone tuberculosis than are the artificial rays, and I wondered whether he had noted any differences in the two forms of light treatment in the production of vitamins.

DR. HOOBLER: There is only one question to be answered, that propounded by Dr. Hess, as to why there is a difference in the potency of vitamin A and vitamin B in mother's milk. That still remains to be determined.

DR. ALFRED F. HESS: Dr. Knox's question, with reference to the comparative value of heliotherapy and light from artificial sources, cannot be answered definitely, but one gets the impression that they have different influences. For instance, we irradiated a group of infants artificially for a period of five months, three times a week, during November, December, January, February and March, and then placed them in the sunlight. The sunlight gave them quite a different color. With the five month's treatment with the mercury vapor quartz lamp the children acquired a brownish color; after the exposure to sunlight they took on a reddish-brown color; the brown seemed to be mixed with red. A difference in the effect of sunlight and the light from the lamp is to be expected, because the spectrum of the lamp and the sun are different. The sun's rays have an extreme length of 300 millimicrons, while the rays of the lamp are 230 millimicrons. There may also be some counteracting influence of the irradiations.

Another question comes up in reference to the point brought up by Dr. Gerstenberger. Dr. Gerstenberger found, and others have found, that if they give cod liver oil it does not enhance the antirachitic value of the milk. If given to the cow cod liver oil does not increase the milk's potency, but if you irradiate a woman it does increase the potency of her milk. When we give cod liver oil, it has to be absorbed and a great deal may be taken by the liver; it has to go through the intermediary metabolic processes and what is left over goes into bone. When irradiation is employed the activated cholesterol goes into the general circulation and the bones gets it directly.

Those who have dairies for human milk and are supplying certified human milk, may in the future supply antirachitic human milk.

DR. CHAPIN: With reference to the Wassermann test, we put the question up to Dr. Park who said the milk was safe if it was pasteurized. If the collection of human milk is carried on in connection with a maternity hospital, it is easy to have the Wassermann test made, but without such a connection and with our shifting population it offers greater difficulties.

The question has been raised: "After all, what good is it?" In the first month of life it is a great help. Statistics show that although infant mortality during the first year has been reduced one half, infant mortality for the first month has been practically untouched. It is due in most cases to congenital

defects and to prematurity. We have had many cases of early prematurity. We had one baby weighing only 2½ pounds and anther of 3½ pounds. Perhaps they are more expert in feeding in St. Louis than we are in New York, but the human milk is a great advantage in the first month and in the premature babies. We have tried to give a demonstration of the way in which human milk could be collected and distributed apart from a maternity hospital, and, with the precautions we use, I believe we can save a certain number of infants who otherwise would be lost.

SOME OBSERVATIONS ON THE ANTIRACHITIC FACTORS IN COD LIVER OIL. Presented by DR. FREDERICK W. SCHLUTZ and DR. MILDRED R. ZIEGLER (by invitation). From the Department of Pediatrics, University of Minnesota, Minneapolis.

An investigation was carried out to determine what causes the appearance and disappearance of the bands characterizing the spectograph of cholesterol. Judging from a former communication (Schlutz, F. W., and Morse, M., *Am. J. Dis. Child.* **30**:199, 1925), it seemed reasonable to expect that the wave lengths which are selectively absorbed, and which disappear on irradiation, are those wave lengths which are effective in activating the cholesterol.

Cholesterol exists in an anhydrous (melting point, 147 C.) and in a hydrated form (melting point, 148.5 C.). Preparations of the former were made by heating in an oven, by sublimation, by precipitation from glacial acetic acid and by crystallization from chloroform or ether. Spectographs of solutions of any of the before-mentioned preparations showed no bands, but great general absorption. The bands were not obscured by the general absorption. This was determined by taking a large number of pictures, in which either the thickness of the solution or the time was varied during the exposure, while one of these factors remained constant.

It has been shown by other investigators that prolonged irradiation will destroy the activity of cod liver oil or activated cholesterol. The question arises whether air is a factor in the destruction of the antirachitic material formed by irradiation. To investigate this, 4 mm. thicknesses of cod liver oil were irradiated in a quartz apparatus for seventeen hours by a mercury vapor quartz lamp. This apparatus consists of three test tubes sealed together at the top. Each tube is provided with an inlet and an outlet. Cod liver oil is placed in the center tube, and water circulates through the innermost and outermost tubes, thus eliminating any effect which might be caused by heat. Cod liver oil irradiated in this apparatus without air, and cod liver oil irradiated in air, was fed to rachitic rats incorporated at 2 per cent by weight in the diet (Steenbock and Nelson, diet 2966) or in 20 drop amounts daily. The oil was not kept for more than forty-eight hours after irradiation before it was administered. The rats received the factor to be tested for periods of ten to sixteen days. The Shipley line test was used to establish the potency of a substance. Cod liver oil irradiated seventeen hours without air, when fed to rats, produced a positive line test. The rats showed a greater average growth than those which received nonirradiated oil. Cod liver oil irradiated seventeen hours in air did not heal rickets. The purified mixture obtained by treating cholesterol with benzoyl peroxide was fed to rats in 20 mg. amounts daily. It produced only slight healing of rickets. The oxidized product is not necessarily the same as the antirachitic factor in cod liver oil. It must be determine whether it is destroyed by irradiation in air.

Thus far, it has not been possible to isolate the material in sufficient quantity from either cod liver oil or the cholesterol derivatives to determine its nature.

There is a possibility that the antirachitic factor could be absorbed material, intimately connected with the chemistry of cholesterol. Work tending to prove this is now in progress.

DISCUSSION

DR. KRAMER: At the present time the antirachitic potency of a substance is tested by adding it in a definite amount to a known rickets-producing diet, and then observing whether it prevents the development of rickets or cures it after

Feeding Experiments with Cod Liver Oil and Oxidized Cholesterol

Rat	Sex	Ration No.	Dietary Addition	Average Food Intake, Gm. per Day	Weight,* Gm.	Dietary Addition Given, Days	Line Test
15	F	2966	.....	5.0	52-74-74	..	Negative
16	M	2966	.....	5.5	60-85-85	..	Negative
23	M	2966	.....	4.6	40-65-68	..	Negative
25	M	2966	Cod-liver oil 2%	5.4	50-72-80	16	Positive
28	F	2966	Cod liver oil 2%	4.0	46-66-70	16	Positive
30	F	2966	Cod liver oil 2%	5.0	40-72-72	12	Positive
36	F	2966	Cod-liver oil 2%	5.5	50-92-92	12	Positive
24	M	2966	Cod-liver oil irradiated 17 hours without air 2%	4.5	60-86-92	16	Positive
26	M	2966	Cod-liver oil irradiated 17 hours without air 2%	4.8	48-72-80	16	Positive
27	M	2966	Cod-liver oil irradiated 17 hours without air 2%	4.9	52-74-80	16	Positive
29	M	2966	Cod-liver oil irradiated 17 hours without air 2%	5.5	52-74-84	16	Positive
33	M	2966	Cod-liver oil irradiated 17 hours without air 2%	5.4	42-64-64	12	Slight healing
34	F	2966	Cod-liver oil irradiated 17 hours without air 2%	5.6	34-60-60	12	Slight healing
35	M	2966	Cod-liver oil irradiated 17 hours without air, 20 drops daily	5.0	52-84-86	12	Positive
39	M	2966	Cod-liver oil irradiated 17 hours without air, 20 drops daily	6.3	58-100-100	12	Slight healing
31	F	2966	Cod-liver oil irradiated 17 hours, 2%	5.8	40-60-56	12	Negative
32	M	2966	Cod-liver oil irradiated 17 hours, 2%	5.9	42-70-63	12	Negative
37	F	2966	Cod-liver oil irradiated 17 hours, 2%	5.4	50-90-84	12	Negative
38	M	2966	Cod-liver oil irradiated 17 hours, 2%	5.6	58-100-100	12	Negative
40	M	2966	Cod-liver oil irradiated 17 hours, 20 drops daily	6.5	60-108-104	12	Negative
20	M	2966	Cholesterol oxidized by benzoyl peroxide	5.6	50-78-80	10	Slight healing
21	M	2966	Cholesterol oxidized by benzoyl peroxide	5.5	50-78-80	10	Slight healing
22	M	2966	Cholesterol oxidized by benzoyl peroxide	5.3	48-73-73	10	Slight healing

* Initial weight; weight when factor to be tested was added; final weight.

it has developed. Those who have worked on this problem will appreciate the importance of a chemical or physical method for the detection or the quantitative estimation of the antirachitic factor. The studies of Schlutz and Morse, as well as those of Hess and his co-workers are, I take it, attempts at the elaboration of such a test.

Drummon and Rosenheim have recently described a color reaction for vitamin A. This test is negative with substances containing vitamin D only.

Dr. Shear, working in our laboratory recently, observed that when a reagent containing aniline and concentrated hydrochloric acid is added to irradiated cholesterol and the mixture is boiled for about half a minute, a red color develops. Highly purified, nonirradiated cholesterol fails to give the color. The same is true of mineral oil, whether irradiated or nonirradiated. Cottonseed and linseed oils give this test only after irradiation. Cod liver oil, nonirradiated, reacts positively both before and after treatment by heat and aeration. Neither methyl alcohol, acetone nor chloroform, the solvents used for cholesterol, give the reaction. The material obtained from the methyl alcohol extract of the irradiated cholesterol also gives the color. This material, which contains some cholesterol, cures rickets in rats when fed at a 2 per cent level. We are not prepared to say that this is a reaction for vitamin D, but the apparent parallelism between the presence of the chromogenic substance and antirachitic potency is so close that if the chromogenic substance is not vitamin D, it certainly seems to be very closely associated with it.

Dr. Alfred F. Hess: I am interested in Dr. Schlutz's observation on cholesterol. I have made experiments as to the activation of linseed oil in air and in nitrogen, and have exposed cholesterol to oxygen. I found no difference, though it may become a little less potent when it is not exposed to oxygen. The difference may be slightly greater if you titrate the material. Dr. Schlutz brought out two points. He irradiated cholesterol as well as cod liver oil for seventeen hours, and when there was no access of air there was developed a positive line test, showing healing in the test animals, whereas when the cod liver oil was irradiated in air there was no healing. In other words, he has shown that we can prevent the destruction of cholesterol following overirradiation by having no access of air. In other experiments it is quite different—cholesterol was oxidized by benzyl peroxide, and when it was fed there was evidence of slight healing.

I was very much interested in what Dr. Kramer said with reference to irradiated cod liver oil, cotton seed oil, mineral oil, and white of egg. I have noted something similar in relation to linseed oil. Linseed oil is yellow, but after it is irradiated it has a reddish color. Although there is this difference, the test did not seem at present to be of practical value as a test for potency.

Dr. Julius H. Hess: You may be interested to learn that Dr. Elizabeth Koch has been able to extract from irradiated cholesterol with liquefied ammonia, a small amount of resinous-like substance which is about fifteen times as active as the irradiated cholesterol itself. This extraction is carried out under pressure in sealed tubes. She used the method of extraction employed by Gustavson in separating the ovarian hormone from cholesterol.

Dr. Alfred F. Hess: I am able to confirm that result as to the solubility of the active fraction of irradiated cholesterol in liquid ammonium.

Dr. Schlutz: It is true that the results with oxidation product of cholesterol were not impressive. We state this fact in the table. The results, however, with cholesterol irradiated without presence of air are very definite and unmistakable. The line test was unquestionably positive.

From the experimental work carried on so far, we have the impression that the antirachitic factor present in cholesterol is in the nature of an adsorbed substance and of course present in very small quantity. The difficulties encountered in attempting to isolate such a substance are well known.

The experimental findings reported by Dr. Kramer are interesting indeed, and may prove a valuable aid in the solution of this difficult problem.

THIRD SESSION

PEDIATRICS IN A MATERNITY HOSPITAL WITH ESPECIAL REFERENCE TO NURSING ROUTINE.* Presented by DR. WALTER LESTER CARR, New York.

In a study of two groups of babies at the Woman's Hospital, consideration was given to the growth, nutrition and well-being of the babies, while the mothers were observed to determine if they were more comfortable when nursing at three or four hour intervals. Attention was paid to the length of time the babies nursed and to their gain while in the hospital. Later, they were seen in the clinic and by the social service nurses. This study was undertaken to encourage mothers to nurse by lessening their discomfort, and to give the babies the best start in nutrition. Hospital routine was simplified by determining the interval most suitable for babies and mothers. The house physicians and nurses gave attention to details of management, and the comparison of the two groups of babies was of practical interest. This study was carried on with the cooperation of Dr. H. R. Mixsell, associated on the service.

Two groups of babies were selected for the three and four series, the smaller babies being put in the first mentioned. The records were compiled by Dr. D. M. Campbell, the resident obstetrician.

In the three hour (breast fed) group there were 150 babies, seventy-four were males, seventy-six were females; the number of primiparous infants was eighty-four and the number of multiparous was 66. The average birth weight of these babies was 7 pounds, 2½ ounces. At the end of fourteen days eighty-seven babies had made a gain of 5 ounces, while sixty-three had lost 5.2 ounces. At the end of one month, 116 babies had gained 1 pound, 11 ounces, while nine babies had lost 5.5 ounces. In the follow-up records, twenty-nine babies who were breast fed weighed at 3 months 14 pounds, 6 ounces and at 6 months 16 pounds, 3 ounces. Eighteen babies who were bottle fed weighed at 3 months 12 pounds, 2.5 ounces, and in 6 months 16 pounds, 8.2 ounces. Of the mixed fed babies, of whom there were eleven, the average weight at 3 months was 14 pounds, 8 ounces and in 6 months 17 pounds, 3 ounces.

In the four hour (breast fed) group there were 150 babies, eighty male and seventy female; the number of primiparous infants was sixty-four, and the number of multiparous was eighty-six. The average birth weight of these babies was 8 pounds, 3¼ ounces. At the end of fourteen days fifty-two babies had gained 3.1 ounces, while ninety-eight babies had lost 6.3 ounces. At the end of one month 113 babies had gained an average of 1 pound, 3 ounces while seven babies had lost an average of 5 ounces. In the follow-up records, eleven babies who were breast fed weighed at 3 months 14 pounds, 7 ounces, and in 6 months 17 pounds, 3¼ ounces. Fourteen babies who were bottle fed weighed at 3 months 12 pounds, 5 ounces, and at 6 months 15 pounds, 7 ounces. Of the mixed fed babies, of which there were five, the average weight at 3 months was 13 pounds, 5 ounces, and in 6 months 17 pounds, 7 ounces.

As many of the mothers had moved away, the figures in the follow-up are from a limited group.

Fifteen babies who were nursed at the breast were observed after five, ten and fifteen minute nursings, and were weighed at the end of each five minutes.

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*From the Clinic of the Woman's Hospital.

The average amount of milk obtained in five minutes by these babies between the fourth and twelfth days was one-eighth ounce. The average amount obtained in ten minutes by the same babies during the same number of days was 2.2 ounces, equal to one-fourth of an ounce addition in the second five minutes. Most of these babies refused all nursing after ten minutes, and when they did take the breast, the amount was seldom more than one-tenth ounce.

The average weight gained by these babies while under observation for eight days was 5.6 ounces.

These figures show similar results to those observed by Smith and Merritt reported to the Society in 1922.

SUMMARY

1. At the end of fourteen days, babies nursed every three hours lead in gain in weight by approximately 2 ounces.

2. In one month, babies nursed every three hours lead in gain in weight by approximately 8 ounces.

3. The initial birth weight of the babies nursed every three hours was 7 pounds, 2½ ounces, compared to 8 pounds, 3¼ ounces of babies nursed every four hours.

4. The breast engorgement and irritation of the nipples were less noticeable when babies were nursed every four hours. The comfort of both the babies and the mothers was superior in the four hour series, and this was recorded particularly by the nursing staff.

5. Jaundice occurred more often in the three hour babies.

6. The actual gain in weight at the end of one month in babies nursed once in four hours was 1 pound, 3 ounces, as compared with the gain of 1 pound, 11 ounces for the babies nursed once in three hours. At the end of six months the average weight of the four hour group, nursed and fed, was 17 pounds, 3.5 ounces, while for the three hours group the average weight was 16 pounds, 3 ounces, so that these babies gained the same amount, 9 pounds, during six months, although the three hour period was used for babies who were a pound lighter in weight than those fed every 4 hours.

DISCUSSION

Dr. De Buys: I want to compliment Dr. Carr on being able to start his work immediately after birth. Undoubtedly, the infant does not come into its own soon enough; the sooner it is recognized that the baby belongs to the pediatrician as soon as the cord is tied, the better for it. We may consider that there are three problems important at this time of life, namely, the body temperature, nutrition and the prevention of infection. In regard to the regulation of body temperature, much can be accomplished in assisting the infant by preventing the loss of body heat, and thus increasing its resistance. The subject is a very large one and cannot be covered in a few minutes. I just want to call attention to one point. Of course the baby does not have an initial bath. We have been able to have a baby go several days without a bath without any harm at all, though usually a bath is given in five or six hours. By not giving the initial bath immediately after birth in a large series of about 300 cases, instead of losing the usual 10 or 11 per cent of their body weight, the babies only lost 8 per cent of their body weight. Instead of the infant

requiring about eleven days to return to its birth weight, it regained its birth weight in eight days. Therefore I believe that some benefit can be derived from paying attention to the baby immediately after birth, and I am convinced that this is one of the observations that confirms that belief.

DR. FRITZ B. TALBOT: I would like to ask if any attempt was made to check the loss of weight after birth. This loss is due to two factors. There is not enough food energy in the colostrum to supply the needs of the baby. It is a well know method to treat new-born babies — it was known for centuries, at least for many years, on the Continent — by giving some form of sugar. Then, as Dr. De Buys has pointed out, the great importance of maintaining the body temperature cannot be overemphasized. If the initial bath is given, the babies' temperature may fall as low as 96 F., and everyone knows that nutrition cannot be maintained and the body will not function normally when the temperature is subnormal. We know that the temperature falls more rapidly the smaller the child, and the necessity therefore is greater of having a higher surrounding temperature to maintain the body temperature at the physiologic temperature. This applies especially to premature infants.

DR. SCHICK: I had an excellent opportunity to make observations along this line in the clinic in Vienna, where there was wholehearted cooperation between the obstetrician and the pediatrician, and I can only point out that it is very important to pay attention to the nutrition of the new-born child, and to avoid infection, particularly if the baby's weight is below 6 pounds. Additional feeding is then very helpful, and it is surprising to see how much better a child looks and feels, and how much more interest it takes in its surroundings, when it is better fed. Furthermore, the danger of infection is important. The mortality in new-born infants is high when catarrhalic infections are prevalent in the city. Many new-born infants die of pneumonia, and it is often said that these children die of weakness, when in reality they die of infection. It should be remembered that pneumonia in new-born children is not accompanied by the usual symptoms. There is often no cough and no elevation of temperature, but at necropsy the lungs are found to be full of extended areas of pneumonia. I was astonished to see how in some maternity hospitals, the children are separated from their mothers, and as many as twenty are placed in one ward. This practice of placing so many new-born children together is dangerous.

DR. CHARLES HENDEE SMITH: Dr. De Buys speaks of the acute loss of heat. Another way the children lose heat is due to the way in which babies' beds are made in most hospitals. In private cases the baby is wrapped in a knitted shawl, while in obstetric hospitals the bed is made in regular hospital style, with sheets and blankets tucked down tight, and often the covers come no higher than the baby's waist. There is more heat lost through these badly made beds than by the bath. The hands being free, the infant finds it easy to start sucking habits. I always insist on having the baby wrapped or swaddled in a blanket or shawl for the first few months. This teaches him to sleep with the arms covered, prevents the loss of heat in the early weeks and the development of colds later on.

DR. KOPLIK: A certain German authority—I have forgotten his name—made an investigation on the relation of conservation of heat and increase in body weight. He found that those exposed to cold did not gain so rapidly; it is my observation that babies discharged from maternity hospitals weighing 6 pounds are given a daily bath. The baby should not be given a daily bath until it weighs 8 pounds.

DR. HEIMAN: A condition we see, especially in maternity hospitals in New York, is infectious impetigo; it has been rather universal in many maternity hospitals. In some instances this infection lead to sepsis neonatorum.

DR. SHERMAN: Some time ago, in the endeavor to have the Buffalo City Hospital and the Buffalo General Hospital place the new-born infants under the care of pediatricians, an attempt was made to decide when an infant was an obstetric case and when a pediatric. I wrote to sixteen institutions, and was surprised to find in one-half the institutions, which were supposed to be unexcelled, that the baby became a pediatric case only when it was ill. In the other half of these institutions the baby became a pediatric case immediately after birth. I have a very strong feeling that the new-born infant should belong to the pediatric department. I think one good work the society can accomplish is to present a united front in definitely concluding that a new-born baby should be turned over to the pediatric department at once, and that the obstetricians should be trained by the same department in the care of the new-born.

DR. HERRMAN: While in the nursery of a maternity hospital the babies are placed in separate cribs, but when they are taken to the mothers for nursing they are all put on a car together, and the danger of infection is still greater. I think the least that could be done would be to put partitions in the car to prevent direct contract.

DR. MORSE: I do not see why the pediatrician should take the baby as soon as it is born. The obstetrician has had and has the care of the mother, and knows better than the pediatrician whether it is advisable for her to nurse her baby. He should know how to feed the baby and how to take care of it. If he does not, he should be taught. To my mind the solution of the problem is education of the obstetrician, not turning the baby over to the pediatrician at once. It should remain with the obstetrician for at least two weeks after it is born. The obstetrician is just as well fitted as the pediatrician to recognize the symptoms of hemorrhagic disease of the new-born and cerebral hemorrhage, for example, and far better fitted to operate if it is necessary. Moreover, he is more in the habit of carrying out the details of asepsis than is the pediatrician.

DR. CHURCHILL: I do not agree with Dr. Morse at all. I have watched obstetricians in two cities. In Chicago they handed the babies over to the pediatrician immediately. If the obstetrician would really watch the baby, there might be something in what Dr. Morse says. My experience, however, is that the obstetrician has no interest in the baby, and furthermore he knows little about it. They hand the baby over to the intern or to the nurse.

DR. VAN INGEN: I would just like to quote what Dr. Holt said on this subject. "Babies are tolerated in maternity hospitals as one of the unavoidable incidents of obstetric practice."

DR. FREEMAN: From what I have seen of the hot nurseries and the warm baths, I think there is little chance that the babies will be chilled.

DR. CARR: While there is some difference of opinion, most of the speakers seem to favor the pediatrician taking care of the baby from birth. Body temperature and the details of bathing should be under careful supervision. The smaller babies should not be bathed but rubbed with albolene or sterile oil, then wrapped up and not disturbed more than necessary. In the matter of infection, we are very particular about any irregularity in temperature. With

reference to what Dr. Schick said about pneumonia, babies died of pneumonia with atelectasis without showing the symptoms of the disease. Impetigo has to be isolated and other babies protected. The alpine lamp promises to be of value in these cases.

I have had the opportunity of seeing new-born babies through the cooperation of the obstetric staff at the Woman's Hospital, and in one institution I am an active member of the medical board, meeting with the obstetric staff. There is no conflict whatever.

JUVENILE DIABETES AND CHRONIC UPPER RESPIRATORY INFECTION. Presented by DR. P. C. JEANS and DR. J. D. BOYD (by invitation).

In the routine care of a group of diabetic children, it was noted that in many the disease was definitely progressing. Increasing amounts of insulin were required from time to time, even though the diet remained constant. It is axiomatic that a continued overstepping of the limits of sugar utilization will lower the tolerance for carbohydrates, but practically all of these patients were under good dietary control. It is well recognized that acute infections decrease the sugar tolerance, and it is reasonable to assume that chronic infection would have a similar effect. Apparently our diabetic patients were not suffering from infections to any unusual degree. The usual physical examination revealed nothing particularly abnormal. The children were exhibiting no noteworthy irregularities in body temperature, nor were they obviously ill in any way, aside from their diabetic condition. In fact, the diabetic group seemed to be a particularly healthy group. Nevertheless, it occurred to us that a careful search for foci of infection would be worth while. Of more than thirty diabetic subjects under observation, twenty-two have been thoroughly examined in regard to upper respiratory infection. The rhinologic examinations were carried out under anesthesia by Dr. L. W. Dean and his assistants. The presence of upper respiratory infection was established in every case.

Eighteen of the patients received local treatment of their infection. This involved the removal of the tonsils and adenoids in practically every instance, and sinus drainage in many cases, supplemented by nasal irrigations and other appropriate measures. The patients so treated showed no apparent ill effects from the therapeutic procedures. Following the operative treatment the body temperature became more nearly constant. In 20 per cent of the treated cases, a definite and even marked lowering of the insulin requirement occurred. Other patients, though requiring the same amount of insulin, reacted to diabetic treatment in a more uniform manner. Previous to operation, the insulin requirement often varied considerably without obvious cause. Following the operative treatment most of the patients became stable as to their insulin requirement, and have remained so. The group showing the most marked improvement was composed entirely of those who had acquired their diabetic manifestations recently. We have gained the impression that, while tonsillectomy may have been beneficial, by far the greatest benefit has been observed as the result of treatment of the sinus infection.

The recognized progressive tendency to inadequacy of carbohydrate handling in diabetic subjects is undoubtedly due, in large part, to the continued overworking of a deficient function. It seems probable, however, that the persistence of the low grade focal infection may also be instrumental in a greater measure than is now usually recognized.

DISCUSSION

DR. HELMHOLZ: I was very much interested in this paper. We have had the opportunity to see a considerable number of cases of diabetes in the childhood period. Our experience with acute infection is that it produces a tremendous lowering of the tolerance of the diabetic subject. We have not, however, attempted to uncover particular foci. Our group of diabetic patients has done unusually well since the introduction of insulin. One patient entered in coma, recovered, then developed pneumonia and again went into coma, recovered, and then had empyema and again went into coma with recovery. A group of cases has been studied by Hempstead and Adams, in which they investigated in adults the relation between infection and insulin tolerance. They found no definite increase in tolerance after removal of foci. They advise, however, that all foci of infection be removed, because any acute exacerbation of infection usually reduces tolerance.

PRIMARY CARCINOMA OF THE LIVER (HEPATOMA) IN CHILDREN. Presented by DR. FRANK C. NEFF, DR. L. P. ENGEL (by invitation) and DR. F. C. HELWIG (by invitation) Kansas City, Mo.

Although primary carcinoma of the liver is rare at any age, not an inconsiderable portion of the proved cases has occurred in infancy and later childhood. Most reports have included all varieties of hepatic malignancies and the differentiation between them not made. Hepatoma is a tumor arising from the parenchymal cells of the liver (which are arranged in columns resembling normal liver structure), bile secretion takes place, and the stroma of the newly formed lobule is composed of capillaries, with some fibrous tissue at its periphery. The growth is unicentric and remains solitary, but metastasis may occur outside of the liver. Liver-cell carcinoma is essentially the type found in childhood.

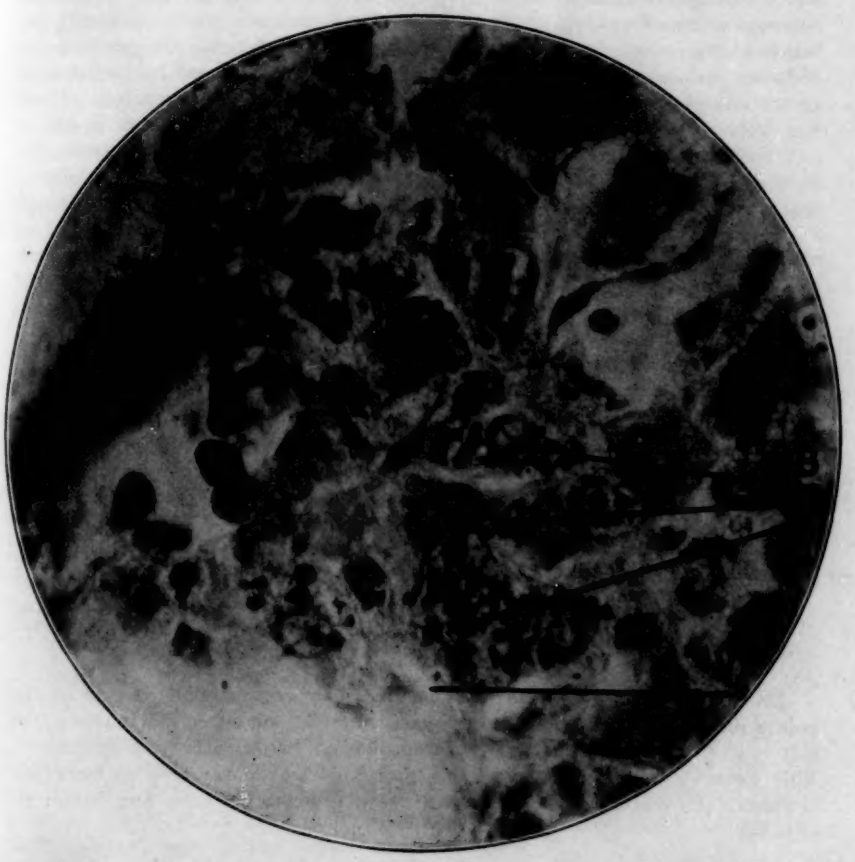
The other form of primary carcinoma is known as cholangioma, originating from the epithelium of the biliary ducts. Its structure is different, showing the attempt to form new bile channels, but no bile is secreted. The stroma is predominantly fibrous and not vascular, as in carcinoma of the liver cell. The liver becomes diffusely and uniformly enlarged.

The writers report a case of their own in a girl, aged 13 years, who was sick for four months. The characteristic clinical findings were the immense, rapidly growing liver, the marked weight loss and the progressive anemia. The atypical symptoms for liver-cell carcinoma were the marked jaundice, the white stools and the ascites, which suggest a complication. A laparotomy was performed in the hope of finding a removable growth. In addition to the large liver, a nodule the side of a small olive was found situated in the common bile duct. The distended gallbladder was drained, and the removal of the common duct obstruction was postponed until the child's condition improved. Postoperative complications were serious, consisting of absence of wound healing, the lengthening of the coagulation of the blood until it would not clot and the final development of peritonitis, from which the child died on the ninth day postoperative.

At necropsy, an irregular tumor nearly half of the size of the right lobe was found in the dome. It was not encapsulated, but had fibrous prolongations into the liver structure. The tumor cells were liver-like in size, shape and arrangement, showing pigment formation, and embedded in a capillary stroma. There was some tendency to fibrosis in the region invaded by the tumor cells.

The mass in the common duct caused obstruction and jaundice. Its minute anatomy showed an extension of the cancerous process from the mother tumor in the liver. An interesting finding was the presence of liver-like cells in an adjacent lymph gland of the transverse fissure. Outside of the liver the only other features of interest were the tendency to visceral and subcutaneous hemorrhages, and a postoperative peritonitis.

The diagnosis and the common theories of etiology are discussed.



Section of tumor tissue characteristic of hepatoma. *B*, bile pigment; *V*, vascular stroma. Throughout are seen the large liver-like cells.

Summarizing, the writers wish to place on record another rare case of hepatoma in a child, especially unusual because of the secondary involvement of the common duct. This type of tumor should be carefully differentiated from malignancies arising in the epithelium of the bile duct.

DISCUSSION

Dr. Julius H. Hess: I want to report a case that came under my observation, with a clinical diagnosis of teratoma of the liver with carcinomatous

degeneration. I am reporting it because of the surgical procedure undertaken to make direct application of roentgen-ray therapy possible. The family had started for Florida in a house built on a Ford truck; they went to Hollywood, where the child was operated on in an improvised hospital. It was thought that he had appendicitis. When the surgeon opened the abdomen, he could not understand why there was so much bloody fluid, as he had ligated all vessels carefully. He found a ruptured appendix. The child made a slow recovery and was brought back to Harvey, Ill. When I first saw the boy he had an enlarged abdomen, ascites and a marked caput medusae. Our diagnosis lay between abscess of the liver and sponge in the abdomen. On opening the abdomen, the same kind of fluid was found as had been noted by the surgeon at the first operation. About a gallon of this fluid was evacuated. There was a large, nodular, cystic tumor and the surgeon, in attempting to lift it out, broke off a large mass of this friable tumor. He decided to suture the borders of the tumor mass to the parietal peritoneum exposing its surface so that roentgen-ray treatment could be instituted, and the rays might be brought into direct contact with the tumor mass. The child received three series of treatments in two weeks, and the mass shrunk to three-fifths its original size, at this time the lower half of the wound was filled by the intestines covered by only a thin layer of peritoneum. The child improved for a period of nine weeks, when he suddenly became worse and the abdomen again filled with fluid. When I left Chicago, the child was practically moribund. This type of surgical procedure was undertaken in the hope that direct exposure to the roentgen rays might give a favorable result.

Note: The child subsequently died, and at necropsy the tumor mass proved to be retroperitoneal. The liver was small and had been displaced upward by the new growth. In all probability the appendix had been the seat of a metastatic tumor.

Observation on the Sickle Cell Phenomenon.* Presented by Dr. Thomas B. Cooley and Dr. Pearl Lee (by invitation). Published in full in this issue.

DISCUSSION

Dr. Friedlander: I want to say a word in confirmation of one of the points just made, and to call attention to one case of sickle cell anemia. In this case there was a basophilic aggregation of 150,000 per cubic millimeter. This figure is aproximately the same that one sees in one type of hemolytic jaundice. It bears out the suggested relation of sickle cells and hemolytic jaundice.

Postoperative Leukocytosis and Temperature Variations Following Tonsillectomy in Children.* Presented by Drs. John A. Foote and Maurice Selinger (by invitation).

In 147 children, aged from 1 to 13, the blood leukocytes were studied before the operation for tonsillectomy, five hours after and twenty-four hours after. The average rectal temperature before operation was found to be 99.3, five hours after operation, 99.6; twenty-four hours after, 99.3. When the data were studied as obtained from children arranged in age groups, the variation in temperature was slight, and such variations as occurred did not parallel the leukocyte changes. The maximum rise in leukocytes was found four or five hours after operation, regardless of the influence of age.

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*From the Children's Hospital, Washington, D. C.

In these 147 children, the average leukocyte count before operation was 11,300; five hours afterward 15,000, and twenty-four hours afterward 14,500. In the children over 7 years of age, the rise of leukocytes five hours after operation approximated the average of 14,500, but twenty-four hours afterward it was 14,875 as compared with 13,725, over 1,000 higher than the average for children younger than 7 years of age. A higher initial leukocyte count was also noticed in children less than 7 years of age, the figures being 12,800 in those less than 7 years of age, as compared with 10.750 in those more than 7. In the age groups below 7 years, a rise of less than 1,000 leukocytes was noticed when the differences between the white cell counts made before operation and twenty-four hours afterward were compared. But in the age groups from 7 to 13, a rise of slightly over 4,000 leukocytes was noticed when the difference between the white cell counts made before operation and twenty-four hours afterward were compared.

While the children in the age groups of 1 to 5, 5 to 7, 7 to 10, 10 to 13 showed a rise of leukocytes amounting to about 3,000 in the first two groups, and 4,000 in the second two groups, those children aged 1 to 5 and 5 to 7 years showed a recession of 2,000 in the leukocyte count twenty-four hours after operation, which amounted to an ultimate increase of about 1,000 over the preoperative count; while the groups of children aged from 7 to 10 and 10 to 13 showed practically no recession, and twenty-four hours after the operation retained their increase of about 4,000 leukocytes over the preoperative leukocyte count.

From the evidence of this series of cases, therefore, an increase of leukocytes of 3,000 to 4,000 may be expected five hours after operation.

In children aged from 1 to 7, twenty-four hours after operation, this increase falls to a figure about 1,000 higher than the preoperative figure; but in children older than this, the increase at this time amounts to 3,000 to 4,000. The leukocyte increase up to twenty-four hours after tonsillectomy has no demonstrable relation to increased temperature.

PEPTIC DIGESTION OF COW'S MILK. THE EFFECT OF VARIOUS MODIFICATIONS USED IN INFANT FEEDING. Presented by DR. JULIUS H. HESS, DR. ELIZABETH M. KOCH (by invitation), and MISS ZELLA C. SENNEWALD (by invitation).

We compared the digestion in vitro of raw certified milk, milk pasteurized at 63 C. for thirty minutes and milk boiled five minutes. We also added to raw certified milk hydrochloric acid, U. S. P. lactic acid, lactic acid cultures, phosphoric acid, lemon and orange juice and the alkalies commonly employed—sodium bicarbonate, sodium citrate and lime water.

Peptic Digestion.—In all the digestion experiments, we added to certified milk or to our milk modifications the equivalent of 30 cc. of tenth normal hydrochloric acid per hundred cubic centimeters of milk plus rennin (2 cc. of 0.2 per cent solution) and pepsin (3 cc. of 0.4 per cent solution). This gave to the plain milk mixtures a p_H of about 4.7. Controls were run on each mixture without pepsin.

For the acid milk modifications, other acids were added in the following proportions: 2.5 cc. of normal hydrochloric acid, 0.8 cc. U. S. P. lactic acid, 2.5 cc. normal phosphoric acid, 2.1 cc. lemon juice and 5.6 cc. orange juice per hundred cubic centimeters of milk. The alkalis were added in the following proportions: 0.43 Gm. sodium citrate, 0.43 Gm. sodium bicarbonate, and 5.5 cc. saturated lime water per hundred cubic centimeters of milk, respectively.

The results of the experiments show that two factors are of prime importance in influencing the amount of soluble protein. The first is the effect of the

treatment or of additions on the solubility of the milk proteins. This is shown in the soluble nitrogen of the controls in which no peptic digestion was involved. Briefly, we found that the solubility of milk proteins was distinctly decreased by boiling and somewhat decreased by lowering the p_H. The soluble proteins of orange juice—milk were markedly increased, byl alkali buffer salts and possibly by other constituents present in the orange juice.

The second factor is the effect of the modifications on peptic digestion. The most important of these modifications are a lowered p_H and denaturization of the proteins such as occurs in boiled milk and cultured lactic acid milk. The greatest increase in soluble nitrogen due to digestion was obtained with cultured lactic acid milk, in which both factors, the lowered p_H and denaturization of the protein were involved. The total soluble nitrogen of the orange juice-milk (that is, the sum of the soluble nitrogen of the controls plus the increase in soluble nitrogen as a result of digestion) was even greater than that of the cultured lactic acid milk.

Alkalinizing milk, although it always increases the soluble protein in the undigested filtrate, inhibits peptic digestion most decidedly. In sodium bicarbonate milk, which is most alkaline, peptic action is completely inhibited.

Egg yolk was added to all of these milk modifications, with no apparent effect on either the soluble nitrogen or peptic digestion.

EFFECT OF ACID AND ALKALI MILKS ON GASTRIC SECRETION

We fed three Pawlow pouch dogs with untreated milk, hydrochloric and acid milks, and the alkali milks. There was no difference either in the volume secreted or in the free or total acidity over a two hour period after feeding with different mixtures.

EFFECT OF MILK MODIFICATIONS ON THE CURD

Young puppies were also fed these milk modifications, and after intervals of one-half and two hours the curd was recovered by vomiting induced by apomorphine. It is of interest that, while in the stomachs of adult dogs, raw milk forms only a custard-like curd, in young puppies the curd is large and inclined to be tough as in human beings. Sometimes 100 cc. of milk was recovered as one large curd.

At the end of one-half hour, hydrochloric acid, lemon juice and orange juice milks were recovered in fine curds about the size of a split pea. With U. S. P. lactic acid milk and cultured milk the curds were like coarse sand. Alkali milks were entirely fluid. This agrees in general with the work of Brennemann.

At the end of two hours the curds remaining in the stomach tend to be firmer and to condense into larger curds. Raw and pasteurized milk curds were so firm that they retained the furrows made by the folds of the gastric or esophageal mucosa. The boiled and acid milk curds were soft enough to break under pressure. The alkali milks were neutralized in two hours and formed distinct curds.

The free and total acidity of the gastric contents at the end of one-half hour were determined in each case. Free acidity was found only when acid milks were fed, and the total acidity was approximately the sum of the normal acidity when raw milk was fed and the acid introduced in the milk. When sodium bicarbonate milk was given, the combined acidity was decreased, probably as a result of volatilization of carbon dioxide after reaction with hydrochloric acid.

At the end of two hours very little fluid was recovered, but the total acidity per cubic centimeter was about the same irrespective of the kind of milk fed,

In the results obtained, the favorable action of orange juice has been repeatedly demonstrated. Lemon and orange juices both introduce vitamins, important mineral constituents and additional alkali buffer salts, and seem to be the logical choice for continued feeding as additions to raw, pasteurized or boiled milk.

Boiling milk definitely reduces its protein content but facilitates gastric digestion.

THE RELATIVE EFFICIENCY OF CERTIFIED AND PASTEURIZED MILK IN INFANT FEEDING. Presented by DR. MAYNARD LADD, MISS HELEN W. EVARTS (by invitation) and MISS LUCILE WILLIAMSON FRANKS (by invitation).

The material studied was drawn from the preventive clinic of the Boston Dispensary, an organization through which is supervised the health of the children who are wards of the Boston Children's Aid Association and the Church Home Society. As many of the children remain under care for several years, they constitute a group from which very accurate data may be had in regard to what actually may be accomplished by intensive health supervision. In a previous paper read before this Society, we have presented the results of medical supervision in foster homes on the mortality rate.

In studying the results obtained in weight development, only babies who were under observation three months or more were included. Two hundred and fifty-nine infants fed during the first year on Grade A milk (pasteurized), without differentiation as to the use of orange juice or cod liver oil, showed an increase of 4.5 per cent over the expected average weight development. Of these children, 201, who were carried for an average of 2.16 years, during the second year, with more varied diets, showed an increase of 11.1 per cent over the expected weight development. Analysis of the clinical histories of a group of fifty-eight babies, who failed to make the expected weight development shows the influence of respiratory infections and exanthemas.

The tabulated results of feeding certified and pasteurized (grade A) milk, with and without orange juice and cod liver oil show strikingly the increasing efficiency of the feeding as orange juice and cod liver oil are added to the pasteurized milk. The expected normal weight development on pasteurized milk was raised 9.5 per cent by the addition of cod liver oil and orange juice. Certified milk, however, exceeded this result, the expected normal weight development being increased 14 per cent, and this without either cod liver oil or orange juice. Its protective properties against rachitic changes were clearly shown by roentgen-ray examinations, made at about three months intervals. It is apparent from these observations that only a very small percentage of babies fed on raw certified milk (without orange juice or cod-liver oil) developed even mild roentgen-ray rachitis of the wrists. These cases (18 per cent of the number observed) were healing or healed at the end of the period of observation. Cases mildly rachitic (by roentgen-ray examination) at the beginning showed healing or healed processes at the end of the period of observation without supplementary doses of orange juice or cod liver oil. The protection and healing properties of the certified milk on rachitic processes was clearly evident. The group of babies fed on grade A pasteurized milk showed a greater incidence of roentgen-ray rachitis at the beginning of the observation, that is, 66 per cent, but with cod liver oil and orange juice, were, without exception, healing or healed at the end. An analysis of the eruption of the teeth, in both series of cases, showed approximately the same curve that occurs in the normal infant as given in Holt's tables.

It is quite possible that the greater efficiency of certified milk over pasteurized milk is due to the more exact and scientific feeding of the cows

in the particular supply of certified milk used and not to the quality of rawness. If this should prove to be the case, it would not necessarily follow that a similar superiority of results over pasteurized milk would obtain in all certified milks. The use of orange juice and cod liver oil as a matter of routine in all babies over 3 months of age, however fed, is, therefore, probably well justified—even though there is reason to believe that the highest grades of certified milk are sufficiently protective; but in our opinion a larger use of certified milk should be encouraged by the medical profession.

DISCUSSION

DR. ALFRED F. HESS: I want to say a word about Dr. Julius Hess' paper. It is very interesting. It is difficult to copy in vitro with any exactness the normal digestion, and to compare it with digestion of infants. For instance, in these experiments you only take cognizance of gastric digestion, but what happened in the intestines we do not know. It would be valuable to know the amount of nitrogen in the stool as well as in the stomach contents. Was the action of these milks on the motility of the stomach considered? The only way to test these various milks satisfactorily is by long continued observation of clinical cases.

Since I suggested lemon juice, I have used it in twenty-five normal babies—that is to say, one ward—continuously, sometimes with the addition of egg yolk and sometimes without any addition. With pasteurized milk we use 3 per cent, or 30 cc. of lemon juice per liter, and in clinical experience find this very satisfactory. Whether it is better than ordinary pasteurized milk it is difficult to say for we cannot judge by the weights. The gastric curd is very soft as we noticed in our original work. In color and consistency, the stools are more nearly similar to the stools of infants fed on breast milk. The results have been satisfactory, but of course we realize that one obtains satisfactory results from other methods. I am glad that these experiments seem to indicate from the theoretic standpoint that the addition of lemon juice is of value.

DR. BRENNEMANN: There was a time when if two as provocative papers as these had been read, it would have been very difficult for the president to know whom to recognize first in the discussion. There seems now to be less excitement and greater unanimity. However, papers such as these it seems to me should be discussed freely. Dr. Hess' paper is very important and very interesting, though deductions from animal experiments and other devices cannot always be applied to human beings. Our babies are not puppies nor guinea-pigs, but are something different. Some years ago I did some experiments along these lines. We started with dogs and gave raw milk. At the end of an hour we chloroformed the dogs and found that no large curd had formed. We then concluded that the dog was not suited to establish the thesis we were interested in at that time. If we could chloroform a baby after a certain interval we could find out more about the condition. There is no satisfactory device by which we can determine the coagulability; vomiting comes nearest to it. Whether inducing vomiting by the use of apomorphine gives us exact information with reference to the curd is a question. Certainly the curds in our human experimentation with apomorphine were much mutilated before they were delivered where we could see them.

One word about the buffer content of milk. It is interesting to go over the experience of the past. Twenty years ago we were all using natural buttermilk or that made with cultures, and German "buttermilk soup" was

very popular. Then a wave of something came from England (we have had many such waves), and we used sodium citrate. I have tried to determine whether I was unusually stupid in using sodium citrate, but it still seems to me that sodium citrate and lime water did do some good in just these cases in which we now use soured milk.

So many factors are involved that it is dangerous to point to one substance and say that that is the one and only thing that makes cow's milk more useful to the baby. Dr. Ladd referred to the value of boiled, pasteurized and certified milk. It is said that "figures do not lie," but the chart at the right might tell an awful story. It would seem to show that certified milk without the addition of cod liver oil and orange juice did better than certified milk with the addition of these two.

DR. GERSTENBERGER: I did not enter the room in time to hear all of Dr. Ladd's paper, and I therefore may be asking unnecessary questions. I cannot understand myself why the infants on the raw milk did not develop rickets. As far as I know, the literature at the present time is 100 per cent unanimous that there is little, if any, antirachitic factor in cow's milk, and that the amount present is not enough to prevent rickets in human infants. I wonder whether Dr. Ladd's infants did not get the antirachitic substance in some other way, possibly egg in the form of cake, or occasional exposure to sunlight. Another reason that makes Dr. Ladd's conclusions seem improbable is the fact that boiling has no destructive effect on the antirachitic factor. McCollum was unable to destroy this factor even by blowing air through hot cod liver oil. It is possible, of course, that certain elements in raw milk may be absorbed better. It is well known that rickets does not develop as readily in infants fed human milk as it does in infants fed cow's milk. This difference, however, is probably not due to any greater presence of antirachitic factor in human milk than in cow's milk, as it is to the peculiar physicochemical make-up of human milk. In all probability the relationship of the protein to the sugar, and sugar to the fat and of the kind of sugar, etc., plays an important rôle. You will recall that Luckhart of Chicago maintained that tetany is due to intestinal toxemia because he was able to remove the symptoms by changing the bacterial flora of the intestinal tract of puppies by feeding large doses of lactose. It is probable that the changed reaction which was produced thereby was responsible for a better absorption of calcium and the consequent improvement in the animals. I think there is no question that rickets develops in normal human infants who are fed cow's milk in the absence of the use of some accepted antirachitic factor.

Further, I doubt the advisability of suggesting the use of raw milk even though it be certified. I recently again had an experience in this connection. Two children developed cervical gland and peritoneal tuberculosis. They had received raw milk from a herd which was tuberculin tested, and which was given care such as is customary in certified dairies. The father of these children finally discovered the source of the trouble, when he picked out for killing the oldest cow, which had always given a negative tuberculin test. The necropsy showed that she was in a very advanced state of tuberculosis, and probably for this reason did not react to the amount of tuberculin used. In my experience, the feeding results obtained with pasteurized milk and with sterilized milk are as satisfactory if not better than with raw milk, and in view of the danger of transmitting an infection by the use of raw milk I do not consider it justifiable to advise its use even though it be certified. Pasteurization or sterilization may tend toward constipation, but constipation is better to have than is tuberculosis.

In connection with Dr. Hess' work, I should like to say that Dr. Nourse and I, during the past few years, have found, while studying growth in puppies, that protein S. M. A. (Acidulated) gives us the best results. This food, in double strength, is quite similar to the chemical composition of bitch's milk. Protein S. M. A. is soured partly by bacterial action and partly by the addition of lemon juice. In other words, we got good feeding results with a milk soured similiarly as was that with which Dr. Hess got fine curd formation. Consequently, our experience seems to corroborate that of Dr. Hess.

Dr. Julius H. Hess: I agree with Dr. Hess about the in vitro experiments They do not reproduce what happens in the human body. We have tried to reproduce peristalsis by rotating the tubes held at 40 to 42 C. We must remember that the mucosa of the stomach is continuously secreting gastric juice, while we added the acid at the beginning of the experiment. As to the intestinal digestion and the action of trypsin, we have not been able to devise anything to represent this. Whether there is anything more than the denaturing of the protein in preparation for tryptic digestion, or whether it is split in advance of tryptic digestion is unknown.

We use the egg yolk and lemon or orange juice a great deal in practice; the babies take them well and thrive. In the experiments we added egg yolk, thinking it might have some colloidal effect in the digestion of protein, but it did not seem to affect digestion one way or the other. So far as digestion is concerned, it is a negative factor.

As to the curds and their removal by apomorphine, and Dr. Brennemann's statement that they must be badly jarred. One of the laboratory workers said to me, "Do not ask me to feed the puppies raw milk and apomorphine again. It took the puppy twenty minutes getting the curd out." If you look at the specimens of curds which I have here, I think you will find that there must have been very little change due to the induced vomiting.

With regard to the sodium citrate, we found that we could feed highly concentrated mixtures, but it is my feeling that I saw a great deal of rickets during the period when I was feedinng 2 grains of sodium citrate, and even when it was reduced to 1 grain to the ounce of milk in the mixtures.

Dr. Ladd: I did not claim that there was no development of rickets. A small percentage of rickets did develop on raw certified milk as it will even in breast-fed infants due to conditions other than diet. But raw certified milk (without orange juice or cod liver oil) has a certain power to prevent rickets, judging from the roentgenograms of the wrists and dentition in this series of cases. Only a small proportion of the number of cases (18 per cent) developed mild rickets on the raw certified milk. The proportion of cases developing rickets on pasteurized milk was considerably larger. The use of the pasteurized milk alone or with orange juice and cod liver oil was simply to determine the relative protective properties of raw milk and pasteurized. There is a definite difference between pasteurized milk and raw certified milk in the effect on nutrition, as shown by weight development. We know that pasteurized milk is not a preventive of rachitis. So far as nutrition is concerned, judging from the weight development, there was a progressive increase in weight as cod liver oil and orange juice were added to the groups receiving pasteurized milk.

As to the use of raw certified milk alone over considerable periods, it is apparent from these observations that the rate of gain is greater, and that only a small proportion of the babies so fed developed even mild rickets of the wrist, which showed healing at the end of the period of observation without supplementary doses of orange juice or cod liver oil.

Book Reviews

INTERNATIONAL MEDICAL ANNUAL, 1926. Pp. 555. Illustrated. Price, $6.00. New York: William Wood & Company.

This is essentially a practical book for the general practitioner. If he wishes to know if there is some new development in the diagnosis or treatment of a disease, he will probably find some helpful reference to it in the book, with bibliography for more intensive reading. It combines the three lines of attack on that common enemy, disease. It refers to the broad principles of preventive medicine, emphasizing predisposing as well as exciting causes; to the new methods of early diagnosis, and to means for the successful treatment of the individual case. The book is conservative in its recommendations, and the following quotation from Sir Humphrey Rolleston seems well worthy of repetition:

"Careful history-taking and a thorough physical examination, with the exhibition of a due proportion of clinical acumen and common sense, will, on the whole, serve the practitioner better than much laboratory lore. But the ideal is a critical judgment founded on the combined information supplied by the two methods, each serving as a supplement and check to the other."

The field of pediatrics is well covered in references to recent work in the diagnosis and treatment of such conditions as hemorrhage and ophthalmia in the new-born, threadworms, poliomyelitis, encephalitis, meningitis, rheumatism, tuberculosis, epilepsy, pyelitis, pyloric stenosis, pertussis, rickets, celiac disease, acidosis, etc.

The book is well illustrated and indexed.

NERVOUS AND MENTAL DISORDERS FROM BIRTH THROUGH ADOLESCENCE. By B. SACHS, M.D., and LOUIS HAUSMAN, M.D. Illustrated. Pp. 861. Price, $10.00. New York: Paul B. Hoeber & Company, 1926.

This is really a revision and elaboration of a former book by Sachs on the same subject, the first chapters having to do with anatomy and embryology and methods of examination. This constitutes Part 1. Part 2 is composed of organic diseases of the nervous system. It begins with a short but useful chapter on diseases of the new-born. Part 3 has to do with functional and toxic diseases; Part 4 with endocrine disorders, vasomotor and trophoneuroses, and Part 5 deals with mental conditions. This book is very definitely the author's, in that it stresses personal opinions strongly. It is rather lacking, if one wishes for an exhaustive discussion of any of these diseases. The first chapter of Part 5 is on the normal child, normal youth development and training. This is a most timely chapter and handled in a most satisfactory and practical manner. It is a chapter which every physician should read, especially if he meets many children in his practice. The following chapter on neuroses and psychoneuroses is also good. On the whole, the book is a good but not exhaustive treatise on the subject, and has many new and interesting features.

THE NORMAL CHILD. ITS CARE AND FEEDING. By ALAN BROWN, M.D. Toronto, McClelland & Stewart, Ltd.

This practical book, "dedicated to the young mothers of Canada," should also find a ready sale on this side of the border. Striving, apparently, for perfection, the author has very ingeniously not only called on his own large experience in pediatrics, but has also used, with proper acknowledgment, material from what he evidently considered the best chapters on various subjects from the best books of other well known pediatricians.

Such a book not only helps a mother to help herself, but also educates her to a better appreciation of so-called preventive pediatrics.

RESEARCH IN PROGRESS AT THE UNIVERSITY OF MINNESOTA, JULY, 1924-JULY, 1925. Compiled by CLARENCE M. JACKSON, M.S., M.D., LL.D. Pp. 306. Price, $1.25. Minneapolis: University of Minnesota.

This book is simply a record of work in progress at the University of Minnesota, including the Mayo Foundation. It is gratifying to see the number of problems being investigated in the realm of pediatrics.